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L34  ANSWER 1 OF 13  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:861431  HCAPLUS
DOCUMENT NUMBER:          134:16550
TITLE:                    Regulation of systemic immune responses utilizing
                          transgenic cytokines and antigens
INVENTOR(S):              Hardy, Steve; Dranoff, Glenn
PATENT ASSIGNEE(S):       Cell Genesys, Inc., USA
SOURCE:                   PCT Int. Appl., 109 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2000072686      A1   20001207       WO 2000-US15190  20000602
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
             CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB,
             GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR,
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KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-324707 A 19990602

AB The authors disclose methodol. for stimulating a prophylactic or therapeutic systemic immune response in a mammal to a tumor. Systemic stimulation is achieved by the administration of a tumor cell expressing retrovirally transduced cytokine(s). In one example, B16 melanoma cells were transduced with the MFG vector expressing interleukin-2 (IL-2). Tumor growth was rejected in mice inoculated with live IL-2-expressing B16, however long-term systemic immunity was absent unless the tumor cells were co-transduced for expression of GM-CSF. In a second example, irradiated B16 cells expressing GM-CSF were shown more capable of mediating the rejection of pre-established tumors than were irradiated cells alone and did not exhibit the toxicity of live transduced B16. In addn., addnl. transfection for interferon-.gamma. compromised the ability of the transduced B16 cells to function as an effective vaccine. The authors also disclose recombinant adenovirus encoding granulocyte-macrophage colony stimulating factor,.

REFERENCE COUNT: 10

REFERENCE(S):
(1) Chiorini; US 5693531 A 1997 HCAPLUS
(2) Dranoff; US 5637483 A 1997 HCAPLUS
(3) Dranoff; US 5904920 A 1999 HCAPLUS
(4) Drayer, J; Developmental Hematology and Immunology 1997, V32, P131 HCAPLUS
(6) Low; US 5837231 A 1998 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:656235 HCAPLUS
DOCUMENT NUMBER: 133:251000
TITLE: MART-1 encoding recombinant vaccinia virus induces a tumor antigen specific immune response
AUTHOR(S): Schutz, A.; Marti, W. R.; Zajac, P.; Spagnoli, G. C.; Jauch, K. W.; Heberer, M.
CORPORATE SOURCE: Klinik und Poliklinik fur Chirurgie der Universitat Regensburg, Regensburg, D-93053, Germany
SOURCE: Chir. Forum Exp. Klin. Forsch. (2000) 45-48
CODEN: CFEKA7; ISSN: 0303-6227
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German

AB Antigen presenting **cells**, infected by MART-127-35 minigene encoding recombinant vaccinia virus, are able to induce a specific HLA-A2.1 restricted immune response. To achieve a larger restriction or an addnl. CD4 stimulation, the authors constructed a recombinant vaccinia virus carrying the MART-1 full length gene. In these expts., the authors compared the relative strength of specific immune stimulation provided by 2 different mol. forms of the same epitope. The sequences of MART-127-35 minigene and MART-1 full length gene were inserted in the vaccinia viral

genome. The recombinant vaccinia virus was rendered replication **incompetent** by treatment with psoralen and long wave UV light. Peptide pulsed or infected HLA.A2 pos. Na-8 **tumor cells**, which do not naturally express MART **tumor** assocd. antigen, were used as target **cells**. MART-127-35 specific CTL were used as effector **cells**. The specific lysis of target **cells** was measured in cytotoxicity assays. The CTL-induction was tested in the cytokine release (IFN-.gamma.ELISA) and 3H-thymidine incorporation in **proliferation** assays. MART-127-35 specific CTL effectively lysed target **cells** infected with MART-127-35 minigene (83% lysis) and MART-1 full length gene (67% lysis) recombinant vaccinia virus. MART-127-35 peptide pulsed target **cells** as a pos. control, showed a specific lysis of 83%. Only MART-127-35 recombinant vaccinia virus was able to induce a significant cytokine release and T-**cell proliferation** ($P < 0.05$). Thus, the relative immunogenicity of a model epitope expressed by viral vectors in 2 different forms was compared. The stronger immune response was induced by **cells** infected with MART-1 minigene recombinant vaccinia virus. However, MART-1 full length gene expressing **cells** were also able to induce an immune response, although weaker as measured by specific lysis, cytokine release and CTL **proliferation**. Nevertheless, an immune response against unknown epitopes and an addnl. CD4 stimulation by intracellular processing of the full length gene could represent advantages of the full length antigen.

REFERENCE COUNT: 6

REFERENCE(S):
(1) Jonathan, L; J Immunol 1997, V158, P2535
(3) Spagnoli, G; Int J Cancer 1995, V64, P309 HCAPLUS
(4) Tsung, K; J Virol 1996, V70(1), P165 HCAPLUS
(5) Zajac, P; Cancer Res 1998, V58(20), P4567 HCAPLUS
(6) Zajac, P; Int J Cancer 1997, V71(3), P491 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:314929 HCAPLUS
DOCUMENT NUMBER: 132:333386
TITLE: Cancer-associated antigens and methods of their identification
INVENTOR(S): Ando, Dale; Chang, Ju-Fay; Mcarthur, James; Roberts, Margo; Simons, Jonathon
PATENT ASSIGNEE(S): Cell Genesys, Inc., USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026676	A1	20000511	WO 1999-US25936	19991103

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,

VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-106795 P 19981103
AB The present invention provides novel, isolated, **tumor**-assocd. antigens, and methods for identifying such antigens in a biol. sample, and of screening for the presence of such an antigen in a biol. specimen, wherein the **tumor** antigen identified reacts with serum from a subject treated with a vaccine comprising a cytokine and **proliferation-incompetent tumor cells** which express the **tumor**-assocd. antigen. Also provided are kits for carrying out the methods of the invention.
REFERENCE COUNT: 4
REFERENCE(S):
(1) Dranoff, G; US 5637483 A 1997 HCAPLUS
(2) Hersey, P; INT J CANCER 1990, V46, P612 MEDLINE
(3) Simons, J; CANCER RESEARCH 1999, V59, P5160 HCAPLUS
(4) Soiffer, R; PROC NATL ACAD SCI USA 1998, V95, P13141 HCAPLUS

L34 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:499011 HCAPLUS
DOCUMENT NUMBER: 129:134918
TITLE: Recombinant Vaccinia virus, an efficient vector system for bioactive human B7-costimulatory molecules
AUTHOR(S): Marti, Walter R.; Schuetz, A.; Oertli, D.; Zajac, P.; Harder, F.; Heberer, M.
CORPORATE SOURCE: Allgemeinchirurgische Klinik, Departement Chirurgie, Kantonsspital Basel, Universitaet Basel, Basel, CH-4031, Switz.
SOURCE: Chir. Forum Exp. Klin. Forsch. (1998) 131-136
CODEN: CFEKA7; ISSN: 0303-6227
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Recombinant Vaccinia viruses (recVV) that express human B7-1 or B7-2 were constructed and tested as a gene expression vector system for delivery of costimulatory function in vitro. All human **tumor cell** lines tested expressed the recombinant mols. upon infection with replication **incompetent** and non-cytopathic recVV B7. **Cell** lines expressing recombinant B7 mols. provided effective co-stimulation for **proliferation** of resting CD4+ T helper **cells** in the presence of suboptimal PMA concns. The co-stimulatory effect was blocked with sol. CTLA-4 proteins. B lymphocytes, which were transformed with Epstein Barr virus and infected with recVV B7-1, overexpressed the co-stimulatory mols. resulting in enhanced co-stimulation. The capacity of these **cells** to stimulate autologous CD4+ memory **cells** of VV immunocompetent donors was not impaired by the recVV, indicating an intact capacity for processing and presenting antigen proteins in the context with MHC class II mols. It was concluded that recVV encoding human B7 mols. were promising exptl. and clin. tools to enhance immune responses.

L34 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:223850 HCAPLUS
DOCUMENT NUMBER: 129:228
TITLE: Antisense c-myc retroviral vector suppresses established human prostate cancer
AUTHOR(S): Steiner, Mitchell S.; Anthony, Catherine T.; Lu, Yi; Holt, Jeffrey T.
CORPORATE SOURCE: Departments of Urology and Cell Biology, Vanderbilt University School of Medicine, Nashville, TN, 37235, USA
SOURCE: Hum. Gene Ther. (1998), 9(5), 747-755
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostate cancer eventually becomes androgen resistant, resumes growth, and kills the patient. Characterization of genetic events that lead to androgen refractory prostatic neoplasia has revealed the frequent overexpression of c-myc and uncontrolled prostate cancer **proliferation**. A novel strategy to combat advanced prostate cancer utilized a replication **incompetent** retrovirus that contained the mouse mammary **tumor** virus (MMTV) promoter within the retroviral vector to allow transcription of antisense c-myc gene within target prostate **tumor cells**. The transduction of cultured DU145 **cells** by XM6:MMTV-antisense c-myc RNA retrovirus did not affect **cell proliferation** in culture, yet a single direct injection of MMTV-antisense c-myc viral media into established DU145 **tumors** in nude mice produced a 94.5% redn. in **tumor** size compared to **tumors** treated with control virus MTMV sense fos and untreated **tumor** by 70 days. Two animals in the antisense c-myc-treated group had complete regression of their **tumors**. Histopathol. examn. of the **tumors** revealed that MMTV-antisense c-myc-transduced DU145 **tumors** had increased **tumor cell** differentiation, decreased invasion, and a marked stromal response. The mechanism for the antitumor effect of MMTV-antisense c-myc retrovirus appears to be suppression of c-myc mRNA and protein, and decreased bcl-2 protein. The in vivo transduction of prostate cancer **cells** with MMTV-antisense c-myc retroviruses reduced **tumor** growth by suppressing c-myc, resulting in the down-regulation of bcl-2 protein. Consequently, the MMTV-antisense c-myc retrovirus may be useful for gene therapy against advanced, hormone-refractory prostate cancer.

L34 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:637310 HCAPLUS
DOCUMENT NUMBER: 127:317792
TITLE: Nonreplicating recombinant vaccinia virus encoding human B-7 molecules elicits effective costimulation of naive and memory CD4+T lymphocytes in vitro
AUTHOR(S): Marti, Walter R.; Zajac, Paul; Spagnoli, Giulio; Heberer, Michael; Oertli, Daniel
CORPORATE SOURCE: Research Unit, Department Surgery, University Hospital Basel, Basel, CH-4031, Switz.
SOURCE: Cell. Immunol. (1997), 179(2), 146-152

CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors constructed recombinant vaccinia viruses (recVV) encoding the human T-**cell** costimulatory mols. B7-1 and B7-2. To abrogate the vaccinia virus transcription termination signal for early genes, the cDNA of B7-1 had to be modified by a T through C sense mutation at position 766. Upon infection with replication **incompetent** and noncytopathic recVV, several **tumor cell** lines as well as cultured human fibroblasts expressed the costimulatory mols. All these **cells** were capable of providing effective costimulation for **proliferation** of resting CD4+T-**cells** after infection with recVV encoding B7 mols. The costimulatory effect could be blocked with CTLA-4 IgG fusion protein, the sol. ligand for B7. RecVV-induced overexpression of B7 on syngeneic EBV-transformed lymphoblastoid B-**cells** was able to costimulate the **proliferative** response of CD4+ memory **cells** against VV antigens. The possibility of easily engineering a variety of human **cells** using recVV encoding human B7 mols. holds implications for the future design of vaccination strategies.

L34 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:18781 HCAPLUS
DOCUMENT NUMBER: 126:58812
TITLE: Non-replicating recombinant vaccinia virus encoding murine B-7 molecules elicits effective costimulation of naive CD4+ splenocytes in vitro
AUTHOR(S): Oertli, Daniel; Marti, Walter R.; Norton, Jeffrey A.; Tsung, Kangla
CORPORATE SOURCE: Dep. Surgery, Washington Univ. Sch. Med., St Louis, MO, 63110, USA
SOURCE: J. Gen. Virol. (1996), 77(12), 3121-3125
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using a series of new insertion/expression vectors, we constructed a set of recombinant vaccinia viruses (recVV) encoding the murine T **cell** costimulatory mols. mB7-1 or mB7-2, or both together in the same construct. On infection with replication **incompetent** and non-cytopathic recVV, several **tumor cell** lines expressed the resp. mols. and bound to CTLA-4. The highest binding capacity was found when both mB7 mols. were co-expressed. Mouse B16.F10 melanoma **cells** expressing mB7-1 or mB7-2 provided effective co-stimulation for **proliferation** of resting CD4+ T **cells** in the presence of Con A and plate-bound anti-T **cell** receptor antibodies, resp. If mB7-1 and mB7-2 were delivered together on the same **cell**, the **proliferative** response of CD4+ T **cells** increased further. The costimulatory effect could be blocked with CTLA-4, the sol. ligand for B7 mols. The possibility of engineering **tumor cells** using recVV holds implications for the future design of vaccination strategies.

L34 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:590601 HCAPLUS
DOCUMENT NUMBER: 125:214276
TITLE: Methods of preparation and use of adenovirus vectors carrying therapeutic genes and their therapeutic uses
INVENTOR(S): Seth, Prem K.; Cowan, Kenneth
PATENT ASSIGNEE(S): The Government of the United States of America, Re, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9625507	A2	19960822	WO 1996-US2336	19960216
WO 9625507	A3	19961107		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR				
AU 9652974	A1	19960904	AU 1996-52974	19960216
PRIORITY APPLN. INFO.:			US 1995-390604	19950217
			WO 1996-US2336	19960216

AB Novel methods of constructing recombinant adenoviral vectors capable of expressing human cDNAs, such as wild-type p53, WAF1/Cip1/p21, p27/kip1, E. coli cytosine deaminase, wild-type p16, TAM 67 (a jun/fos dominant neg. mutant) and B7-1 and B7-2 are described. The method uses an adaptation of the ClaI method for prepg. encapsidation-**incompetent** virus. A virus carrying a second ClaI site that is useful in the excision of the 5'-region of the viral genome is constructed for use in the method. The invention further provides methods of inhibiting the **proliferation** of **cells**, inhibiting the **cell** cycle of **proliferating cells**, and methods for the eradication of **cells**, esp. cancer and diseased **cells**, by infecting the **cells** with a recombinant adenovirus vector capable of expressing human cDNAs. Compns. and methods of the invention are suitable for treatment of a subject afflicted with a **tumor** wherein the **cells** of the **tumor**, for example, lack the wild-type p53 allele and/or process a mutated p53 gene. The invention addnl. provides a method for the use of adenoviral vectors in the treatment of cancer **cells**, such as lung cancer and breast cancer **cells**. The invention further provides methods for the use of adenoviral vectors in cancer gene therapy as a mechanism for purging bone marrow **cells** of contaminating **tumor cells**, for eradicating cancer **cells**, and for preventing development of cancer **cells** and **tumors**. The construction of an expression vector for the expression of the wild-type p53 gene and its use to inhibit the **proliferation** of breast cancer-derived **cell** lines is demonstrated.

L34 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:916215 HCAPLUS
DOCUMENT NUMBER: 123:336037
TITLE: Expression of cell cycle regulatory factors in differentiating osteoblasts: postproliferative up-regulation of cyclins B and E
AUTHOR(S): Smith, Elisheva; Frenkel, Baruch; Schlegel, Robert; Giordano, Antonio; Lian, Jane B.; Stein, Janet L.; Stein, Gary S.
CORPORATE SOURCE: Dep. Cell Biol. Cancer Cent., Univ. Massachusetts Med. Cent., Worcester, MA, 01655, USA
SOURCE: Cancer Res. (1995), 55(21), 5019-24
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The representation of cyclins and cyclin-dependent kinases (cdks) was analyzed during progressive development of the bone **cell** phenotype in cultures of normal diploid rat calvarial osteoblasts. Three developmental stages were examd.: (a) **proliferation**; (b) monolayer confluency; and (c) mineralization of the bone extracellular matrix. We demonstrate that the presence of cyclins and cdks is not restricted to the **proliferation** period. Consistent with their role in **cell** cycle progression, cdc2 and cdk2 decrease postproliferatively. However, cdk4 and cyclins A, B, and D1 persist in confluent **cells**. Cyclin E is significantly up-regulated during the extracellular matrix mineralization developmental period. Examn. of the cytoplasmic levels of these **cell** cycle regulatory proteins indicates a marked increase in cyclin B in the late differentiation stage. The elevation of nuclear cyclin E and cytoplasmic cyclin B is not obsd. in osteoblasts maintained under culture conditions that do not support differentiation. Furthermore, treatment with transforming growth factor .beta. for 48 h during the **proliferation** period renders the **cells incompetent** for differentiation and abrogates the postproliferative up-regulation of cyclins B and E. D.-induced growth inhibition of ROS 17/2.8 osteosarcoma **cells** is not accompanied by up-regulation of nuclear cyclin E and cytoplasmic cyclin B when compared to the **proliferation** period. This observation is consistent with abrogation of both growth control and differentiation regulatory mechanisms in **tumor cells**. These results suggest that **cell** cycle regulatory proteins function not only during **proliferation** but may also play a role in normal diploid osteoblast differentiation.

L34 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:628622 HCAPLUS
DOCUMENT NUMBER: 121:228622
TITLE: Nitric oxide is an important mediator for tumoricidal activity in vivo
AUTHOR(S): Farias-Eisner, Robin; Sherman, Michael P.; Aeberhard, Ernesto; Chaudhuri, Gautam
CORPORATE SOURCE: Dep. Obstetrics Gynecolofy, Pediatrics, Molecular Medical Pharmacology, University of California, Los Angeles, CA, 90024-1740, USA

M. Smith 308-3278

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1994), 91(20), 9407-11
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB When cultured in vitro, peritoneal macrophages, obtained from mice previously inoculated with bacillus Calmette-Guerin, release nitric oxide, which is cytostatic and/or cytolytic for **tumor cells**. However, it is not known whether nitric oxide has antitumor effects in vivo. Here the authors demonstrate that nitric oxide is an important mediator of host resistance to syngeneic and xenogenic ovarian **tumor** grafts in C3HeB/FeJ mice. A murine ovarian teratocarcinoma **cell** line, utilized to study the mechanism of bacillus Calmette-Guerin-induced host resistance to a syngeneic ovarian **tumor, proliferated** when transplanted i.p. Marked **tumoricidal** activity was obsd., however, when these murine ovarian teratocarcinoma **cells** were transplanted 8 days after i.p. bacillus Calmette-Guerin inoculation. In studies related to xenogeneic ovarian **tumor** grafts, **tumoricidal** activity was obsd. after i.p. transplantation of a human epithelial ovarian cancer **cell** line, NIH:OVCAR-3. This **cell** line **proliferates** only in athymic nude (immunol. **incompetent**) mice. In both sets of expts., **tumoricidal** activity was reduced by inhibition of nitric oxide synthesis. These results demonstrate the **tumoricidal** action of nitric oxide in vivo.

L34 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:161242 HCAPLUS
DOCUMENT NUMBER: 120:161242

TITLE: Transfer and expression of the human interleukin-4 gene in carcinoma and stromal cell lines derived from lung cancer patients

AUTHOR(S): Hunt, Jay D.; Pippin, Barbara A.; Landreneau, Rodney J.; Jacob, William F.; Lotze, Michael T.; Siegfried, Jill M.
CORPORATE SOURCE: Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: J. Immunother. Emphasis Tumor Immunol. (1993), 14(4), 314-21
CODEN: JIEIEZ; ISSN: 1067-5582
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Introduction of the interleukin-4 (IL-4) gene into **cells** derived from human **tumor** tissue provides a means for generating a specific **tumor** vaccine. Such a vaccine could be produced by either transducing **tumor**-derived stromal **cells** with the IL-4 vector and co-injecting **tumor cells**, or by transducing the **tumor cells** themselves. The authors have developed a protocol for culturing **cells** from non-small **cell** lung **tumors** and routinely produce **tumor** cultures from 25% of **tumors**, and stromal cultures from > 80% of specimens. Several of these cultures were transduced with the **incompetent** retroviral vector G1NaSvi4.25, which encodes the human IL-4 cDNA and the G418-resistance gene. Infection of **cells** by

viral titers of 2-5.times.104 plaque-forming units/mL, and a moi of 0.1:1 to 1:1 yielded transfer efficiencies of 3.3-32.0 transfectants per 104 **cells** in six of eight attempts. Following selection with the neomycin analog G418, IL-4-producing **cells** were isolated. IL-4 titers ranged from 142 to 593 U/mL/106 in a 24-h collection. Successful transfer of the IL-4 gene was demonstrated by polymerase chain reaction amplification of cDNA derived from reverse-transcribed total RNA, by immunohistochem., and by ELISA. The IL-4-producing **cells** were shown to stimulate the **proliferation** of autologous peripheral blood lymphocytes in one individual by 7.5-fold over control and by 4.1-fold over non-IL-4 producing **tumor cells**. Gene transfer was performed between 18 and 60 days after acquisition for stromal **cells** and within 150 days for **tumor cells**. **Cells** from lung cancer patients may have potential for generating **tumor** vaccines. In addn., use of lung **tumor**-derived stromal **cells** for transfection may have some advantages over dermal fibroblasts for use in gene therapy.

L34 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:79081 HCAPLUS
DOCUMENT NUMBER: 118:79081
TITLE: Interleukin-6 undergoes transition from paracrine growth inhibitor to autocrine stimulator during human melanoma progression
AUTHOR(S): Lu, Chao; Kerbel, R. S.
CORPORATE SOURCE: Div. Cancer Res., Sunnybrook Health Sci. Cent., Toronto, ON, M4N 3M5, Can.
SOURCE: J. Cell Biol. (1993), 120(5), 1281-8
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability to penetrate the dermal basement membrane and subsequently **proliferate** in the underlying mesenchyme is one of the key steps in malignant progression of human melanomas. Previously studies were undertaken aimed at assessing how normal dermal fibroblasts (one of the main **cellular** components of mesenchyme) may affect the growth of human melanoma **cells** and facilitate the overgrowth of malignant subpopulations (Cornil, I., et al., 1991). Melanoma **cell** lines from early-stage (metastatically **incompetent**) lesions were growth inhibited whereas those from advanced-stage (metastatically competent) evidently were stimulated under the same conditions by co-culture with fibroblasts; conditioned medium from such **cells** gave the same result. Subsequent studies using biochem. purifn. and neutralizing antibodies revealed the inhibitory activity to be identical to interleukin-6 (IL-6). Now is reported that addn. of purified recombinant human IL-6 resulted in a growth inhibition in vitro by G1/G0 arrest of early, but not advanced stage melanoma **cells**. Despite this alteration in response there was no difference in melanoma **cell** lines of varying malignancy in respect to their expression of genes encoding the IL-6 receptor, or gp130, the IL-6 signal transducer. Scatchard anal. also revealed similar [125I]IL-6 binding activities in both IL-6 sensitive and resistant groups. However, studies of IL-6 prodn. indicated that 5 out of 8 IL-6 melanoma **cell** lines known to be resistant to exogenous IL-6-mediated growth inhibition constitutively

expressed mRNA for IL-6; they also secreted bioactive IL-6 into culture medium. To assess the possible role of this endogenous IL-6 in melanoma **cell** growth, antisense oligonucleotides to the IL-6 gene were added to cultures of melanoma **cells**. This resulted in a growth inhibition only in **cell** lines that produced endogenous IL-6. In contrast, neutralizing antibodies to IL-6 were ineffective in causing such growth inhibition. This indicates that endogenous IL-6 may behave as a growth stimulator by an intracellular (private) autocrine mechanism. Thus, a single cytokine, IL-6, can switch from behaving as a paracrine growth inhibitor to an autocrine growth stimulator within the same **cell** lineage during malignant **tumor** progression. Such a switch may contribute to the growth advantage of metastatically competent melanoma **cells** at the primary or distant organ sites and thereby facilitate progression of disease.

L34 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:631894 HCAPLUS
DOCUMENT NUMBER: 117:231894
TITLE: Interleukin 6: a fibroblast-derived growth inhibitor of human melanoma cells from early but not advanced stages of tumor progression
AUTHOR(S): Lu, Chao; Vickers, Mark F.; Kerbel, Robert S.
CORPORATE SOURCE: Div. Cancer Res., Sunnybrook Health Sci. Cent., Toronto, ON, M4N 3M5, Can.
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1992), 89(19), 9215-19
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently the authors reported that human dermal fibroblasts, or conditioned media obtained from such **cells**, affect the growth of human melanoma **cells** as a direct function of **tumor** progression: melanoma **cells** obtained from early-stage (metastatically **incompetent**) primary lesions were growth inhibited, whereas **cells** obtained from more advanced (metastatically competent) primary lesions, or metastases, were growth stimulated. Ion-exchange and gel-filtration chromatog. of fibroblast conditioned medium revealed the inhibitor to be a protein of mol. mass between 20 and 30 kDa and distinct from the stimulator. This is the approx. mol. mass of interleukin 6 (IL-6), a ubiquitous multifunctional cytokine known to affect in particular many kinds of hemopoietic and lymphoid **cells**. Since this cytokine is known to be made by fibroblasts, the authors attempted to det. if the human fibroblast-derived growth inhibitor (hFDGI) was identical to IL-6. Neutralizing antibodies specific for IL-6 completely eliminated the inhibitory activity of hFDGI. Moreover, exposure to human recombinant IL-6 was found to inhibit the growth of early-stage melanoma **cells** obtained from radial growth phase (RGP) or early vertical growth phase (VGP) primary lesions in three of four cases. In contrast, melanoma **cells** from a no. of more advanced VGP primary lesions, or from distant metastases, were completely resistant to this IL-6-mediated growth inhibition. Acquisition of an IL-6-resistant phenotype by metastatically competent melanoma **cell** variants may provide such **cells** with a **proliferative** advantage within the dermal mesenchyme (a hallmark of melanoma

cells that are malignant), helping them eventually to dominate advanced primary lesions and to establish secondary growths elsewhere.

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=> d stat que
L12           3 SEA FILE=REGISTRY (GM-CSF/CN OR "GM-CSF RECEPTOR (HUMAN
                .ALPHA.-SUBUNIT SOLUBLE 3)"/CN OR "GM-CSF/IL-2 INHIBITION
                FACTOR (ORF VIRUS STRAIN NZ-2 GENE GIF)"/CN)
L18        2569 SEA FILE=REGISTRY TUMOR?(L) ASSOCIATED(L) ANTIGEN?
L23             SEL  L12 1- CHEM :      19 TERMS
L24       10933 SEA FILE=HCAPLUS L23
L25       10950 SEA FILE=HCAPLUS L24 OR GM(W)CSF OR GRANULOCYTE(W)MACROPHAGE?(W
                )COLONY(W)STIMULATING(W)(FACTOR? OR ACTIVIT?) OR MACROPHAGE(W)G
                RANULOCYTE(W)CSF
L30        1413 SEA FILE=HCAPLUS L18 OR (TUMOR OR TUMOUR)(W)ASSOCIATED(W)ANTIGE
                N?
L34          13 SEA FILE=HCAPLUS PROLIFERAT?(L)INCOMPETENT(L)TUMOR?(L)CELL?
L37           5 SEA FILE=HCAPLUS L25 (L)L30
L38           5 SEA FILE=HCAPLUS L37 NOT L34


=> d ibib abs hitrn l38 1-5

L38  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        1999:443193  HCAPLUS
DOCUMENT NUMBER:         131:212795
TITLE:                   Dendritic cells infiltrating tumors cotransduced with
                         granulocyte/macrophage
                         colony-stimulating factor
                         (GM-CSF) and CD40 ligand genes
                         take up and present endogenous tumor-
                         associated antigens, and prime naive
                         mice for a cytotoxic T lymphocyte response
AUTHOR(S):               Chiodoni, Claudia; Paglia, Paola; Stoppacciaro,
                         Antonella; Rodolfo, Monica; Parenza, Mariella;
                         Colombo, Mario P.
CORPORATE SOURCE:        Department of Experimental Oncology, Istituto
                         Nazionale per lo Studio e la Cura dei Tumori, Milan,
                         20133, Italy
SOURCE:                  J. Exp. Med. (1999), 190(1), 125-133
                         CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER:               Rockefeller University Press
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   We transduced BALB/c-derived C-26 colon carcinoma cells with
     granulocyte/macrophage colony-stimulating factor (GM-CSF) and CD40 ligand
     (CD40L) genes to favor interaction of these cells with host dendritic
     cells (DCs) and, therefore, cross-priming. Cotransduced cells showed
     reduced tumorigenicity, and tumor take was followed by regression in some
     mice. In vivo tumors were heavily infiltrated with DCs that were
     isolated, phenotyped, and tested in vitro for stimulation of
     tumor-specific cytotoxic T lymphocytes (CTLs). BALB/c C-26 carcinoma
     cells express the endogenous murine leukemia virus (MuLV) env gene as a
     tumor-assocd. antigen. This antigen is shared among solid tumors of
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BALB/c and C57BL/6 mice and contains two epitopes, AH-1 and KSP, recognized in the context of major histocompatibility complex class I mols. H-2Ld and H-2Kb, resp. DCs isolated from C-26/GM/CD40L tumors grown in (BALB/c .times. C57BL/6)F1 mice (H-2d.times.b) stimulated interferon .gamma. prodn. by both anti-AH-1 and KSP CTLs, whereas tumor-infiltrating DCs (TIDCs) of BALB/c mice stimulated only anti-AH-1 CTLs. Furthermore, TIDCs primed naive mice for CTL activity as early as 2 d after injection into the footpad, whereas double-transduced tumor cells required at least 5 d for priming; this difference may reflect direct DC priming vs. indirect tumor cell priming. Immunohistochem. staining indicated colocalization of DCs and apoptotic bodies in the tumors. These data indicate that DCs infiltrating tumors that produce GM-CSF and CD40L can capture cellular antigens, likely through uptake of apoptotic bodies, and mature in situ to a stage suitable for antigen presentation. Thus, tumor cell-based vaccines engineered to favor the interaction with host DCs can be considered.

REFERENCE COUNT: 44

REFERENCE(S):
(1) Albert, M; J Exp Med 1998, V188, P1359 HCAPLUS
(2) Albert, M; Nature 1998, V392, P86 HCAPLUS
(3) Albert, M; The Immunologist 1998, V6, P194 HCAPLUS
(4) Allione, A; Cancer Res 1994, V54, P6022 HCAPLUS
(5) Armstrong, C; Cancer Res 1996, V56, P2191 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:565292 HCAPLUS

DOCUMENT NUMBER: 129:314747

TITLE: Immunopathology of metastases in patients of colorectal carcinoma treated with monoclonal antibody 17-1A and granulocyte macrophage colony-stimulating factor

AUTHOR(S): Shetye, Jayant; Ragnhammar, Peter; Liljefors, Maria; Christensson, Birger; Froedin, Jan-Erik; Biberfeld, Peter; Mellstedt, Haekan

CORPORATE SOURCE: Department of Oncology/Pathology [J. S., P. R., M. L., J-E. F., P. B.], Stockholm, S-17176, Swed.

SOURCE: Clin. Cancer Res. (1998), 4(8), 1921-1929
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Twenty patients with metastatic colorectal carcinoma were treated with a single infusion (400 mg) of a mouse monoclonal antibody (IgG2a) against the tumor-assocd. antigen CO 17-1A and with a daily injection of granulocyte macrophage colony-stimulating factor (GM-CSF) for 10 days. The cycle was repeated every month. Metastases from 5 of the 20 patients biopsied on days 1 and 10 of the first two treatment cycles were studied by immunohistochem. During treatment, neutrophils, monocytes, and T lymphocytes increased concordantly in the tumor as in the blood of the individual patient. Macrophages (CD68) and CD8+ T cells infiltrated the tumor glands and displayed TIA-1-reactive cytotoxic granules. Neutrophils were seen mainly in areas of necrosis. Activated (HLA-DR+) CD4+ T cells were usually abundant in the stroma. During treatment, few natural killer cells were found in the tumor, contrary to the marked increase seen in

blood. Our observations indicate that GM-CSF markedly recruited activated, tumor-infiltrating leukocytes, possibly representing antibody-dependent cellular cytotoxicity and cytotoxic T effector cells. The notion that combined antibody and GM-CSF therapy may also promote a T-cell antitumor response is further supported and advocated by our findings. The study lends further support to combining GM-CSF with monoclonal antibody-based therapy.

L38 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:205543 HCAPLUS
DOCUMENT NUMBER: 128:307276
TITLE: Therapeutic effects on experimental metastatic tumor-bearing mice by vaccination with GM-CSF gene-modified and tumor antigen-pulsed macrophages
AUTHOR(S): Yu, Yizhi; Cao, Xuetao; Lei, Hong; Zhang, Minghui; Zhang, Weiping; Zhu, Xuejun; Ye, Tianxing; Wang, Jianli
CORPORATE SOURCE: Dep. Immunology, Second Military Med. Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Sci. China, Ser. C: Life Sci. (1998), 41(1), 107-112
CODEN: SCCLFO; ISSN: 1006-9305
PUBLISHER: Science in China Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Macrophages, with potent cytotoxic and antigen-presenting activities, can be used in cancer treatment. The biol. characteristics and antitumor effect of GM-CSF could be detected in the supernatants of macrophages after gene transfer. The cytotoxicity and the expression of MHC class II mols. of the gene-modified macrophages increased significantly and the antigen-presenting ability was enhanced. The gene-modified macrophages were then pulsed with tumor antigen and used to treat the exptl. pulmonary metastatic mice. The no. of pulmonary metastases was reduced significantly and the cytotoxicity of the CTL induced from the splenocytes of the tumor-bearing mice also increased. The results demonstrated that adenovirus-mediated GM-CSF gene transfer can activate macrophages to some extent and GM-CSF gene-modified, antigen-pulsed macrophages may be a new type of effective effector cells in the immunogene therapy of cancer.

L38 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:643864 HCAPLUS
DOCUMENT NUMBER: 127:314481
TITLE: Enhanced antitumor effects of tumor antigen-pulsed dendritic cells by their transfection with GM-CSF gene
AUTHOR(S): Cao, Xuetao; Zhang, Weiping; Ma, Shihua; Zhang, Minghui; Wang, Jianli; Ye, Tianxing
CORPORATE SOURCE: Dep. Immunol., Second Military Med. Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Sci. China, Ser. C: Life Sci. (1997), 40(5), 539-545
CODEN: SCCLFO; ISSN: 1006-9305
PUBLISHER: Science in China Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To investigate the biol. characterization and antitumor activities of GM-CSF gene-transfected dendritic cells, the splenic dendritic cells were

infected with GM-CSF recombinant replication-deficient adenoviruses in vitro. Their enhanced expression of B7 was demonstrated by FACs anal., and more potent stimulatory activity was confirmed by allogeneic MLR. Immunization of dendritic cells pulsed with irradiated B16 melanoma cells induced significant CTL and enabled host to resist the challenge of wild-type B16 cells. When they were transfected with GM-CSF gene subsequently, the induced CTL activity was higher, and the produced protection against B16 cell challenge and therapeutic effect on the mice with preestablished pulmonary metastases more effective. These data suggest that the dendritic cells pulsed with tumor antigen then transfected with GM-CSF gene can be used as an effective vaccine in tumor immunotherapy.

L38 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:58343 HCAPLUS
DOCUMENT NUMBER: 124:97723
TITLE: Vaccination of cancer patients using **tumor-associated antigens** mixed with interleukin-2 and **granulocyte-macrophage colony stimulating factor**
INVENTOR(S): Elliott, Robert L.; Head, Jonathan F.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5478556	A	19951226	US 1994-202516	19940228

AB A breast cancer vaccine which comprises a mixt. of tumor assocd. antigens (TAA) with low doses of recombinant interleukin-2 (IL-2) and granulocyte-macrophage colony stimulating factor (GM-CSF).

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L10 94 SEA FILE=REGISTRY ANTIBOD?/CN
L11 66 SEA FILE=REGISTRY MONOCLONAL ANTIBOD?/CN
L18 2569 SEA FILE=REGISTRY TUMOR?(L) ASSOCIATED(L) ANTIGEN?
L20 323186 SEA FILE=HCAPLUS L10 OR ANTIBOD?
L21 98197 SEA FILE=HCAPLUS L11 OR (MONOCLONAL(W)ANTIBOD? OR MAB#)
L22 598147 SEA FILE=HCAPLUS L20 OR AB#
L30 1413 SEA FILE=HCAPLUS L18 OR (TUMOR OR TUMOUR)(W)ASSOCIATED(W)ANTIGEN?
L39 132 SEA FILE=HCAPLUS (TEST? OR ASSAY? OR DIAG? OR DETERM? OR DETN? OR SCREEN?)(L)L30
L40 92 SEA FILE=HCAPLUS L39 AND (L20 OR L21 OR L22)
L42 4 SEA FILE=HCAPLUS L40 AND ELECTROPHOR?

=> d ibib abs hitrn 142 1-4

M. Smith 308-3278

L42 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:487387 HCAPLUS
DOCUMENT NUMBER: 131:126415
TITLE: Human tumor-associated gene HOJ-1 and its diagnostic and therapeutic applications
INVENTOR(S): Hoon, David S. B.
PATENT ASSIGNEE(S): John Wayne Cancer Institute, USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937771	A1	19990729	WO 1999-US1395	19990122
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9924662	A1	19990809	AU 1999-24662	19990122

PRIORITY APPLN. INFO.:		
US 1998-72126	A1	19980122
US 1999-234685	A	19990121
WO 1999-US1395	W	19990122

AB The present invention describes a novel tumor marker antigen encoded by a gene designated as HOJ-1. HOJ-1 was discovered by using the two-hybrid yeast system in which the bait protein was human MAGE-1. The cDNA sequences isolated from a human testis cDNA library is 888 bp in length and codes for a protein 109 amino acids in length. The closest related sequence belongs to the potential oncogene HRC1 and is only 64% nucleic acid homol. RT-PCR studies indicated by gel **electrophoresis** that normal cells, except testis and placenta, do not express HOJ-1, whereas multiple carcinoma cell lines and biopsies express HOJ-1 at different frequencies. In specific embodiment, the nucleic acid sequences disclosed herein are for use in the diagnosis and prognosis of cancer. Also provided are related protein and **antibody** compns. and various methods of use thereof, including methods for cancer diagnosis and treatment.

IT **233265-63-9**
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; human tumor-assocd. gene HOJ-1 and its **diagnostic** and therapeutic applications)

IT **222948-86-9**, GenBank U82396
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleotide sequence; human tumor-assocd. gene HOJ-1 and its

diagnostic and therapeutic applications)
REFERENCE COUNT: 2
REFERENCE(S): (1) Hoon, D; DATABASE EMBL - R57U005 Entry/Accno U82396 1998
(2) Marra, M; DATABASE EMBL - EMEST19 Entry MMA68103 Accno AA068103

L42 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:42621 HCAPLUS
DOCUMENT NUMBER: 130:109202
TITLE: Method for identification of cellular protein antigens and presence of **antibodies** to specific cellular protein antigens in serum
INVENTOR(S): Hanash, Samir M.; Misek, David; Hinderer, Robert; Prasanan, Latha
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900671	A2	19990107	WO 1998-US13295	19980626
WO 9900671	A3	19990610		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882673	A1	19990119	AU 1998-82673	19980626
EP 991945	A2	20000412	EP 1998-932884	19980626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-50832 19970626
WO 1998-US13295 19980626

AB The present invention relates to a method for identification of cellular protein antigens to which patients with cancer, or patients at risk for cancer, may develop autoantibodies. The method of the invention involves the use of patient derived sera for the identification of the cellular protein antigens using two-dimensional gel **electrophoresis** followed by Western Blot anal. The identification of such protein antigens provides novel markers that can be utilized for screening, for diagnostics and prognosis of disease. The invention also provides for the use of the identified protein antigens in immunoassays designed to detect the presence of serum **antibodies** to the specific protein antigens in sera from individuals that may harbor such **antibodies** . The invention further relates to the use of the identified antigens as immunogens for stimulation of an immune response in patients expressing

such protein antigens. The invention is demonstrated by way of example in which elevated levels of circulating autoantibodies reactive against a tumor specific antigen were identified in sera derived from a lung cancer patient. In addn., elevated levels of circulating autoantibodies reactive against several specific .beta.-tubulin isoforms were detected in the sera of neuroblastoma patients.

L42 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:115363 HCAPLUS
DOCUMENT NUMBER: 128:166365
TITLE: Isolated protein which binds to A33 **antibody**, and peptides corresponding to portions of the protein
INVENTOR(S): Old, Lloyd J.; Welt, Sydney; Ritter, Gerd; Simpson, Richard J.; Nice, Edouard; Moritz, R. L.; Catimel, B.; Ji, Hong; Burgess, Anthony W.; Heath, Joan K.; White, Sara J.; Johnstone, Cameron
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: U.S., 38 pp. Cont.-in-part of U. S. 511,876, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5712369	A	19980127	US 1996-597495	19960202
WO 9708189	A1	19970306	WO 1996-US12699	19960805
W: AU, CA, IL, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2229028	AA	19970306	CA 1996-2229028	19960805
AU 9667650	A1	19970319	AU 1996-67650	19960805
AU 701105	B2	19990121		
EP 851870	A1	19980708	EP 1996-928049	19960805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11511973	T2	19991019	JP 1996-510274	19960805

PRIORITY APPLN. INFO.: US 1995-511876 19950804
US 1996-597495 19960202
WO 1996-US12699 19960805

AB This invention relates to isolated protein and to peptides which are found on the surface of colon cells and colon cancer cells, as well as to nucleic acid mols. encoding said protein and peptides. The protein and peptides bind to tumor-assocd. **antibodies**, such as **mAb** A33. The monomeric protein has a mol. wt. of about 43 kD as detd. by SDS gel **electrophoresis** under non-reducing conditions. In addn., this invention relates to the use of said nucleic acid mols., protein, in monomeric or multimeric form, and to **antibodies** to said peptides in diagnostic, screening and therapeutic methods. This invention further relates to **antibodies** specific for said protein, in monomeric or multimeric form, and to **antibodies** to said peptides.

IT **187414-72-8 188573-18-4**, Antigen A33 (human)

RL: PRP (Properties)
(amino acid sequence; colon or colon cancer-assocd. surface protein and peptides which binds to A33 **antibody** for **diagnosis** and treatment of cancer)

L42 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1983:591091 HCAPLUS
DOCUMENT NUMBER: 99:191091
TITLE: Identification and purification of human lung **tumor-associated antigens** (hLTAA) and clinical detection and **determination** of these antigens
INVENTOR(S): Braatz, James Anthony; McIntire, Kenneth Robert; Princler, Gerald Lee
PATENT ASSIGNEE(S): United States, Dept. of Defense, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8303008	A1	19830901	WO 1983-US181	19830210
W: AU, JP				
RW: AT, BE, CH, DE, FR, GB, NL, SE				
US 351588	A0	19821105	US 1982-351588	19820223
US 4514506	A	19850430	US 1983-462022	19830128
AU 8313390	A1	19830908	AU 1983-13390	19830210
JP 59500287	T2	19840223	JP 1983-501000	19830210

PRIORITY APPLN. INFO.:
US 1982-351588 19820223
US 1983-462022 19830128
WO 1983-US181 19830210

AB A method is described for the affinity immunoadsorption purifn. of human lung tumor-assocd. antigen (hLTAA I and II) specific to human lung tumors of diverse histol. characteristics and for its use in the detn. of hLTAA in blood serum by immunoassay, e.g. RIA. The purifn. method involves ion-exchange chromatog. and/or gel filtration of crude lung tumor ext. followed by solid-phase affinity immunoadsorption on the purified IgG fraction of adsorbed xenoantiserum raised against a pool of crude lung tumor ext. and covalently coupled to a solid support. At all stages of purifn., the product is assayed for hLTAA, e.g. by radial immunodiffusion. RIA was carried out by using 125I-labeled hLTAA and sepn. of bound and free antigen with Pansorbin, or by sandwich solid-phase RIA and sepn. by using a 2nd **antibody**. The RIA is useful in detg. hLTAA levels <1 .mu.g/mL. Thus, hLTAA was purified from human lung carcinoma tissue by chromatog. of the crude ext. on DEAE-cellulose, elution with a linear NaCl gradient, gel filtration on Sephadex G 200, and affinity chromatog. on CNBr-activated Sepharose 4B coupled to the IgG fraction from rabbit antiserum R-152 and elution with thiocyanate. The purity of the hLTAA was monitored by SDS-polyacrylamide gel **electrophoresis**. The purified hLTAA was characterized by gel **electrophoresis**, high-performance liq. chromatog., isoelec. focusing, gel filtration, and

sedimentation velocity, and labeled with 125I by using the Bolton-Hunter reagent.

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=> d stat que
L13           1 SEA FILE=REGISTRY "SODIUM DODECYL SULFATE"/CN
L14           1 SEA FILE=REGISTRY POLYACRYLAMIDE/CN OR "POLYACRYLAMIDE
                RESIN"/CN
L15          15 SEA FILE=REGISTRY POLYACRYLAMIDE?/CN
L16          15 SEA FILE=REGISTRY L14 OR L15
L18        2569 SEA FILE=REGISTRY TUMOR?(L) ASSOCIATED(L) ANTIGEN?
L26             SEL  L13 1- CHEM :     174 TERMS
L27      102378 SEA FILE=HCAPLUS L26
L28       20186 SEA FILE=HCAPLUS (L27 OR SDS OR SODIUM(W)DODECYL(W)SULFATE?)(5A
                )(POLYACRYLAMIDE? OR L16)
L30        1413 SEA FILE=HCAPLUS L18 OR (TUMOR OR TUMOUR)(W)ASSOCIATED(W)ANTIGE
                N?
L43      160997 SEA FILE=HCAPLUS PROTEIN?(L)((MOL OR MOLECULAR)(W)(WEIGHT OR
                WT) OR MW OR DALTON? OR KDA)
L44       20001 SEA FILE=HCAPLUS (L28 OR GEL(W)ELECTROPHOR?) AND L43
L45          15 SEA FILE=HCAPLUS L44 AND ((CANCER OR TUMOR OR TUMOUR)(W)ASSOCIA
                TED(W)(ANTIGEN? OR AG) OR L30)


=> d ibib abs hitrn l45 1-15

L45  ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:314929  HCAPLUS
DOCUMENT NUMBER:          132:333386
TITLE:                    Cancer-associated antigens
                          and methods of their identification
INVENTOR(S):              Ando, Dale; Chang, Ju-Fay; Mcarthur, James; Roberts,
                          Margo; Simons, Jonathon
PATENT ASSIGNEE(S):       Cell Genesys, Inc., USA
SOURCE:                   PCT Int. Appl., 94 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2000026676      A1   20000511       WO 1999-US25936  19991103
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,
             VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 1998-106795   P  19981103
AB   The present invention provides novel, isolated, tumor-assocd. antigens,
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and methods for identifying such antigens in a biol. sample, and of screening for the presence of such an antigen in a biol. specimen, wherein the tumor antigen identified reacts with serum from a subject treated with a vaccine comprising a cytokine and proliferation-incompetent tumor cells which express the tumor-assocd. antigen. Also provided are kits for carrying out the methods of the invention.

REFERENCE COUNT: 4
REFERENCE(S):
(1) Dranoff, G; US 5637483 A 1997 HCAPLUS
(2) Hersey, P; INT J CANCER 1990, V46, P612 MEDLINE
(3) Simons, J; CANCER RESEARCH 1999, V59, P5160 HCAPLUS
(4) Soiffer, R; PROC NATL ACAD SCI USA 1998, V95, P13141 HCAPLUS

L45 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:396129 HCAPLUS
DOCUMENT NUMBER: 131:227372
TITLE: Construction and characterization of a chimeric fusion protein consisting of an anti-idiotype antibody mimicking a breast **cancer-associated antigen** and the cytokine GM-CSF
AUTHOR(S): Tripathi, Pulak K.; Qin, Hongxing; Bhattacharya-Chatterjee, Malaya; Ceriani, Roberto L.; Foon, Kenneth A.; Chatterjee, Sunil K.
CORPORATE SOURCE: Department of Internal Medicine, Division of Hematology and Oncology and The Lucille Parker Markey Cancer Center, University of Kentucky Medical Center, Lexington, KY, 40536, USA
SOURCE: Hybridoma (1999), 18(2), 193-202
CODEN: HYBRDY; ISSN: 0272-457X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Anti-idiotype antibody, 11D10 mimics biol. and antigenically a distinct and specific epitope of the high **mol. wt.** human milk fat globule (HMFG), a cancer-assocd. antigen present in over 90% of breast tumor samples. To augment the immunogenicity of 11D10 without the aid of a carrier **protein** or adjuvant, the authors made a chimeric 11D10-GM-CSF fusion **protein** for use as a vaccine. An expression plasmid for 11D10 was made by ligation of the DNA sequences of the 11D10 light-chain variable region upstream of the human .kappa. const. region. The heavy-chain plasmid carrying GM-CSF was made by ligation of the heavy-chain variable region sequences upstream of the human .gamma.1 const. region CH1 fused to the DNA fragment encoding the mature GM-CSF peptide 3' to the CH3 exon. NS1 plasmacytoma cells were transfected with the light and heavy-chain vectors by electroporation. Fusion **protein** secreted in the culture medium was purified and was characterized by **gel electrophoresis** as well as by detn. of the biol. activity of the fused GM-CSF. In nonreducing **SDS-polyacrylamide** gels, a single band .apprx.200 Kd reacted with anti-human .kappa., anti-human .lambda.1 and anti-GM-CSF antibodies. In reducing polyacrylamide gels, a .apprx.74 **kDa protein** reacted with anti-human .lambda.1 and anti-GM-CSF antibodies. The fusion **protein** induced proliferation of GM-CSF

dependent NFS-60 cells. These results suggest that the **protein** is a chimeric anti-idiotype antibody consisting of 11D10 variable domains, human .kappa. and .lambda.1 const. domains and that the GM-CSF moiety fused to the const. region .lambda.1 is biol. active.

REFERENCE COUNT: 41

REFERENCE(S):
(1) Altschul, S; J Mol Biol 1990, V215, P403 HCAPLUS
(2) Arnaout, M; J Clin Invest 1986, V78, P597 HCAPLUS
(4) Bhattacharya-Chatterjee, M; J Immunol 1987, V139, P1354 HCAPLUS
(5) Bhattacharya-Chatterjee, M; J Immunol 1990, V145, P2758 HCAPLUS
(6) Blanchard, D; J Leukoc Biol 1991, V50, P28 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:115363 HCAPLUS

DOCUMENT NUMBER: 128:166365

TITLE: Isolated protein which binds to A33 antibody, and peptides corresponding to portions of the protein

INVENTOR(S): Old, Lloyd J.; Welt, Sydney; Ritter, Gerd; Simpson, Richard J.; Nice, Edouard; Moritz, R. L.; Catimel, B.; Ji, Hong; Burgess, Anthony W.; Heath, Joan K.; White, Sara J.; Johnstone, Cameron

PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA

SOURCE: U.S., 38 pp. Cont.-in-part of U. S. 511,876, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5712369	A	19980127	US 1996-597495	19960202
WO 9708189	A1	19970306	WO 1996-US12699	19960805
W: AU, CA, IL, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2229028	AA	19970306	CA 1996-2229028	19960805
AU 9667650	A1	19970319	AU 1996-67650	19960805
AU 701105	B2	19990121		
EP 851870	A1	19980708	EP 1996-928049	19960805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11511973	T2	19991019	JP 1996-510274	19960805

PRIORITY APPLN. INFO.: US 1995-511876 19950804
US 1996-597495 19960202
WO 1996-US12699 19960805

AB This invention relates to isolated **protein** and to peptides which are found on the surface of colon cells and colon cancer cells, as well as to nucleic acid mols. encoding said **protein** and peptides. The **protein** and peptides bind to tumor-assocd. antibodies, such as mAb A33. The monomeric **protein** has a **mol. wt.** of about 43 kD as detd. by SDS **gel electrophoresis**

under non-reducing conditions. In addn., this invention relates to the use of said nucleic acid mols., **protein**, in monomeric or multimeric form, and to antibodies to said peptides in diagnostic, screening and therapeutic methods. This invention further relates to antibodies specific for said **protein**, in monomeric or multimeric form, and to antibodies to said peptides.

IT **187414-72-8 188573-18-4**, Antigen A33 (human)
RL: PRP (Properties)
(amino acid sequence; colon or colon cancer-assocd. surface protein and peptides which binds to A33 antibody for diagnosis and treatment of cancer)

L45 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:270725 HCAPLUS
DOCUMENT NUMBER: 126:250217
TITLE: Colon cell and colon cancer cell associated nucleic acid molecules, protein and peptides
INVENTOR(S): Welt, Sydney; Ritter, Gerd; Simpson, Richard J.; Nice, Edouard; Moritz, R. L.; Catimel, Bruno; Ji, Hung; Burgess, Antony; Heath, Joan; White, Sara; Johnston, Cameron; Old, Lloyd J.
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA; Welt, Sydney; Ritter, Gerd; Simpson, Richard J.; Nice, Edouard; Moritz, R., L.; Catimel, Bruno; Ji, Hung; Burgess, Antony; et al.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9708189	A1	19970306	WO 1996-US12699	19960805
W: AU, CA, IL, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5712369	A	19980127	US 1996-597495	19960202
AU 9667650	A1	19970319	AU 1996-67650	19960805
AU 701105	B2	19990121		
EP 851870	A1	19980708	EP 1996-928049	19960805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11511973	T2	19991019	JP 1996-510274	19960805

PRIORITY APPLN. INFO.: US 1995-511876 19950824
US 1996-597495 19960202
WO 1996-US12699 19960805

AB This invention relates to isolated **protein** and to peptides which are found on the surface of colon cells and colon cancer cells, as well as to nucleic acid mols. encoding said **protein** and peptides. The **protein** and peptides bind to tumor-assocd. antibodies, such as mAb A33. The monomeric **protein** has a **mol. wt.** of about 43 kD as detd. by SDS **gel electrophoresis** under non-reducing conditions. In addn., this invention relates to the

use of said nucleic acid mols., **protein**, in monomeric or multimeric form, and to antibodies to said peptides in diagnostic, screening and therapeutic methods. This invention further relates to antibodies specific for said **protein**, in monomeric or multimeric form, and to antibodies to said peptides.

IT **188573-18-4**, Antigen A33 (human)
RL: PRP (Properties)
(amino acid sequence; colon cell and colon cancer cell assocd. nucleic acid mols., protein and peptides)

IT **187414-72-8**
RL: PRP (Properties)
(colon cell and colon cancer cell assocd. nucleic acid mols., protein and peptides)

L45 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:532248 HCAPLUS
DOCUMENT NUMBER: 125:191420
TITLE: Presence in bovine fetal serum of the protein antigenically related to p65-**tumor associated antigen**: Its isolation and polyclonal antibody production
AUTHOR(S): Mirowski, M.; Walaszek, Z.; Hanausek, M.
CORPORATE SOURCE: Institute Environmental Research and Bioanalysis, Medical University, Lodz, 90-151, Pol.
SOURCE: Neoplasma (1996), 43(2), 83-88
CODEN: NEOLA4; ISSN: 0028-2685
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monoclonal antibodies raised to the 65-**kDa** tumor-assocd. **protein** (p65) isolated from a human breast cancer cell line have been used to detect an antigenically related **protein** (p65-like) present in fetal bovine serum (FBS) by Western blot anal. We have isolated the p65-like **protein** from FBS by isoelectrofocusing (IEF) on native gels followed by electrophoresis in 12.5% **polyacrylamide** gel contg. 0.1% **SDS** (**SDS**-PAGE). Immunostaining with anti-p65 monoclonal antibody of fetal bovine serum fractions sepd. by electrophoresis on cellulose acetate membrane revealed that the p65-like **protein** had a location similar to one of .gamma.-globulin. This **protein** migrates as a single band upon electrophoresis in SDS-PAGE and had four isoforms which migrate as two doublets with pI's of approx. 5.0 and 5.3.

L45 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:207800 HCAPLUS
DOCUMENT NUMBER: 118:207800
TITLE: Molecular cloning and expression of a transformation-sensitive human protein containing the TPR motif and sharing identity to the stress-inducible yeast protein STI1
AUTHOR(S): Honore, Bent; Leffers, Henrik; Madsen, Peder; Rasmussen, Hanne H.; Vandekerckhove, Joel; Celis, Julio E.
CORPORATE SOURCE: Inst. Med. Biochem., Aarhus Univ., Aarhus, DK-8000, Den.

SOURCE: J. Biol. Chem. (1992), 267(12), 8485-91
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A transformation-sensitive human **protein** (IEF SSP 3521) that is 2-fold up-regulated in SV40-transformed MRC-5 fibroblasts has been purified by two-dimensional **gel electrophoresis,** microsequenced, and its cDNA cloned using oligodeoxyribonucleotides. The 2.1-kilobase cDNA encodes a 543-amino acid **protein** with a calcd. mol. mass of 62.6 **kDa** and a calcd. pI of 6.77. Expression of the cDNA in AMA cells using the vaccina virus expression system followed by two-dimensional **gel electrophoresis** showed that the **protein** comigrated with IEF SSP 3521. The **protein** contains the tetratricopeptide repeat found in families of fungal **proteins** required for mitosis and RNA synthesis. In particular, the **protein** has 42% amino acid sequence identity to STI1, a stress-inducible mediator of the heat shock response in Saccharomyces cerevisiae. Northern blot anal. indicated that the IEF SSP 3521 mRNA is up-regulated in several transformed cells. Immunofluorescence studies using a polyclonal antibody raised against the purified **protein** revealed that the antigen is present mainly in the nucleus of SV40-transformed MRC-5 fibroblasts, while it localizes to the Golgi app. and small vesicles in their normal counterparts. The possible physiol. role of IEF SSP 3521 is discussed in the light of its structural relationship with STI1.

IT **142361-67-9,** GenBank M86752
RL: PRP (Properties)
(nucleotide sequence of)

L45 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:146693 HCAPLUS
DOCUMENT NUMBER: 104:146693
TITLE: Immunoprecipitation of a Mr 64,000 glial **tumor -associated antigen** by monoclonal antibody 217c
AUTHOR(S): Luner, Stephen J.; De Vellis, Jean
CORPORATE SOURCE: Fac. Med., Dalhousie Univ., Halifax, NS, B3H 4H7, Can.
SOURCE: Cancer Res. (1986), 46(2), 863-5
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monoclonal antibody 217c binds to a tumor-assocd. surface antigen of transformed rat glial cells. Treatment of C6 glioma cells with 2.5% 1-butanol yielded an ext. which was active in competitive inhibition of antibody 217c to cell monolayers in an 125I-labeled **protein** A assay as well as in binding antibody 217c in an enzyme-linked immunodot assay. The antigen, however, was not released in sol. form, but in a particulate fraction which could be pelleted by ultracentrifugation for 2 h at 120,000 .times. g. Antibody binding activity in the immunodot assay could be destroyed by heating the ext. to 100.degree. for 10 min. To det. the **mol. wt.** of the antigenic polypeptide, cell monolayer cultures were surface radioiodinated and extd. with Nonidet P-40. Immobilized antibody 217c bound only a single labeled polypeptide with a **mol. wt.** of 64,000 as detd. by **SDS**

polyacrylamide gel electrophoresis. This surface peptide was present in the C6 glioma line as well as in oligodendrocyte and astrocyte cultures transformed either spontaneously or using ethylnitrosourea. It was absent from normal astrocyte and oligodendrocyte cultures of neonatal rat brain. In the glial lines studied the P-64 peptide appears as a surface marker indicating malignant transformation.

L45 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:539974 HCAPLUS
DOCUMENT NUMBER: 103:139974
TITLE: Production and characterization of mouse monoclonal antibodies to human bladder **tumor-associated antigens**
AUTHOR(S): Young, Deborah A.; Prout, George R., Jr.; Lin, Chi Wei
CORPORATE SOURCE: Urol. Res. Lab., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
SOURCE: Cancer Res. (1985), 45(9), 4439-46
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monoclonal antibodies (McAbs) to human bladder carcinoma were generated by fusion of NS-1 mouse myeloma cells with spleen cells from BALB/c mice immunized with either cultured human bladder cancer cells or cells obtained from a fresh surgically removed bladder tumor. Four hybridomas which reacted strongly with bladder tumor cells and not to normal skin fibroblasts or urothelial cells were identified and cloned by limiting diln. to obtain monoclonality. One McAb, 3G2-C6, raised with cultured tumor bladder cells MGH-U1 (EJ) as the immunogen reacted more strongly to the bladder tumor lines tested than any of the other McAbs. Hybridoma 3G2-C6 secreted murine IgG1 and produced high titer ascites fluid when grown in BALB/c mice. Results from quant. enzyme-linked immunosorbent assays on a panel of >35 cell lines demonstrated that McAb 3G2-C6 reacted with several bladder tumor cell lines 50-90-fold more than with normal transitional urothelium. Two kidney and 2 testicular tumor lines also bound 10-fold more 3G2-C6 than with normal cells. The 3G2-C6 antigen was only marginally detected on a no. of other cancer and noncancerous cells. To identify the antigen, 125I-labeled membrane components from MGH-U1 cells were extd. with detergent, immunopptd. with **protein** A-bound 3G2-C6, and analyzed by SDS-**gel electrophoresis**. This revealed that McAb 3G2-C6 binds to a 90,000 **mol. wt.** cell surface component. Indirect immunofluorescence microscopy with fluorescein isothiocyanate-anti-mouse IgG also identified the antigen on the surface of cultured and fresh tumor cells and detected the antigen on 16 of 17 Grade 3 bladder tumor specimens as well as on some kidney and testicular tumor cells. This study confirms the potential of the hybridoma technique for producing McAbs capable of identifying tumor assocd.-antigens which may be useful in the diagnosis and treatment of bladder cancer.

L45 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:111058 HCAPLUS
DOCUMENT NUMBER: 102:111058
TITLE: Purification and characterization of a pancreas

cancer-associated antigen from normal colonic mucosa

AUTHOR(S): Kitada, Masashi; Mori, Takesada; Shimano, Takashi; Maruyama, Hirohide; Kosaki, Goro

CORPORATE SOURCE: Med. Sch., Osaka Univ., Osaka, 553, Japan

SOURCE: Clin. Chim. Acta (1984), 144(2-3), 173-83
CODEN: CCATAR; ISSN: 0009-8981

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pancreas cancer-assocd. antigen (PCAAc) was extd., isolated, and purified from human normal colonic mucosa. Purified PCAAc from normal colonic mucosa was homogeneous, as detd. by polyacrylamide disc **gel electrophoresis**. The PCAAc had a **mol. wt.** of approx. 600,000 and consisted of 30% carbohydrate and 70% **protein**. It had an isoelec. point of 4.4, and migrated to the .alpha.2-.beta. region on immunoelectrophoresis. It was apparently different from other known gastrointestinal mucus antigens. Antiserum against purified PCAAc did not react with normal human serum, pancreas, liver, spleen, or lung, but did react with ascites fluid from a patient with pancreatic cancer. PCAAc appears to be a mucus antigen that is assocd. with pancreatic cancer.

L45 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1984:405212 HCAPLUS

DOCUMENT NUMBER: 101:5212

TITLE: Purification and partial characterization of a murine mammary **tumor-associated antigen**

AUTHOR(S): Chattopadhyay, Joya; Chatterjee, Ramdas; Chattopadhyay, Utpala; Chowdhury, Jayasree Roy

CORPORATE SOURCE: Dep. Tumor Immunobiol., Chittaranjan Natl. Cancer Res. Cent., Calcutta, 700 026, India

SOURCE: Gann (1984), 75(4), 334-41
CODEN: GANNA2; ISSN: 0016-450X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A mammary tumor-assocd. antigen (MTAA) from the murine mammary tumor virus (MuMTV)-induced mammary tumors of C3H/J mice was purified and partially characterized. The crude ext. of the mammary tumor, when subjected to DEAE-cellulose chromatog. and eluted with a discontinuous NaCl gradient, provided 3 major **protein** peaks, of which only the first (F1) possessed the MTAA activity. The antigen was further purified by subjecting F1 to polyacrylamide **gel electrophoresis**. The MTAA was a glycoprotein with a **mol. wt.** of approx. 83,000. The antigen was localized in the plasma membrane and was different from the MuMTV structural antigens. Circulating antibodies against the MTAA were obsd. in the sera of tumor-bearing mice but not in that of tumor-free mice.

L45 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1984:101303 HCAPLUS

DOCUMENT NUMBER: 100:101303

TITLE: Studies of a melanoma **tumor-associated antigen** detected in the

spent culture medium of a human melanoma cell line by allogeneic antibody. III. Physicochemical properties
AUTHOR(S): Gupta, Rishab K.; Morton, Donald L.
CORPORATE SOURCE: Sch. Med., UCLA, Los Angeles, CA, 90024, USA
SOURCE: JNCI, J. Natl. Cancer Inst. (1984), 72(1), 83-92
CODEN: JJIND8; ISSN: 0198-0157
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A melanoma tumor-assocd. antigen (TAA), isolated from spent culture medium of human melanoma cell line UCLA-SO-M14, was purified to mean homogeneity to det. its phys. and biochem. nature. Gel filtration and native polyacrylamide **gel electrophoretic** analyses of the 125I-labeled melanoma TAA revealed that the antigen had a **mol. wt.** in the range of 180,000-190,000. However, ultracentrifugation of melanoma 125I-labeled TAA in a 5-20% sucrose d. gradient revealed a sedimentation coeff. of 4.96. Melanoma 125I-labeled TAA focused at a pH of 6.5 by isoelec. focusing. No carbohydrates were detectable by various colorimetric methods in the highly purified melanoma TAA fraction, and melanoma TAA failed to bind with several lectins. Its antigenic activity was destroyed by proteolytic enzymes but was not affected by glycosidic enzymes or phospholipase A2. The melanoma TAA was most likely a lipoprotein. The **protein** portion apparently formed the antibody binding sites(s).

L45 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:459797 HCAPLUS
DOCUMENT NUMBER: 95:59797
TITLE: Two human **tumor-associated antigens**, p155 and p210, detected by monoclonal antibodies
AUTHOR(S): Loop, S. M.; Nishiyama, K.; Hellstrom, Ingegerd; Woodbury, Richard G.; Brown, J. P.; Hellstrom, Karl Erick
CORPORATE SOURCE: Div. Tumor Immunol., Fred Hutchinson Cancer Res. Cent., Seattle, WA, 98104, USA
SOURCE: Int. J. Cancer (1981), 27(6), 775-81
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BALB/c mice were immunized with human melanoma cells and their spleen cells hybridized with NS-1 myeloma cells. The hybrids were screened for the prodn. of antibodies that bound to melanoma cells. Two hybridomas of interesting specificity were identified and cloned. Hybridoma 5.1 produces an IgG1 antibody that binds to about half of the melanomas and carcinomas tested. The target is a polypeptide with an apparent **mol. wt.** of 210 kilodaltons on **SDS-polyacrylamide gel electrophoresis**. The antigen, denoted p210, is also expressed in normal adult brain and in certain fetal tissues. Hybridoma 6.1 produces an IgM antibody that binds to about 50% of the melanomas, and 80% of the kidney carcinomas tested. The antigen defined by this antibody in melanomas has an apparent **mol. wt.** of 155 kilodaltons and is denoted p155. It has not been obsd. on any normal adult or fetal tissues. The antigen present in the kidney carcinomas was not p155, but rather consisted of 2

proteins of approx. 60,000 and 250,000-300,000 **daltons**. This observation suggests the possibility that the antigenic determinant recognized by antibody 6.1 may be present on several distinct **protein** mols.

L45 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:154701 HCAPLUS
DOCUMENT NUMBER: 94:154701
TITLE: Identification, purification, and radioimmunoassay of NB/70K, a human ovarian **tumor-associated antigen**
AUTHOR(S): Knauf, Suzanne; Urbach, Gerald I.
CORPORATE SOURCE: Dep. Obstetr. Gynaecol., Univ. Toronto, Toronto, ON, Can.
SOURCE: Cancer Res. (1981), 41(4), 1351-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB NB/70K, a tumor-assocd. antigen of human ovarian epithelial tumor Fraction OCA, was purified and identified as a glycoprotein which is stable in 0.6M HClO4, binds to concanavalin A, and migrates electrophoretically with .alpha.-like mobility in barbital-buffered agarose at pH 8.6. NB/70K does not appear to contain normal serum, normal ovary, normal lung, or carcinoembryonic antigen-like cross-reacting antigenic determinants as measured by radioimmunoassay. NB/70K was purified from ovarian antigen Fraction OCA by chromatog. on .gamma.-globulin coupled to Sepharose 4B and by elution from acrylamide gels. NB/70K migrates as a single band with an apparent **mol. wt.** of 70,000 in SDS-acrylamide **gel electrophoresis**. A rabbit antibody raised against NB/70K pptd. a polypeptide with a **mol. wt.** of 70,000 as visualized by autoradiog. of SDS-acrylamide gels. A radioimmunoassay was developed for measuring NB/70K activity, using Staphylococcus aureus **protein** A as a pptg. agent.

L45 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:81902 HCAPLUS
DOCUMENT NUMBER: 94:81902
TITLE: **Tumor-associated antigens** in spent medium of human melanoma cells: immunochemical characterization with xenoantiserums
AUTHOR(S): Galloway, D. R.; McCabe, R. P.; Pellegrino, M. A.; Ferrone, S.; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. and Res. Found., La Jolla, CA, 92037, USA
SOURCE: J. Immunol. (1981), 126(1), 62-6
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Xenoantisera to human melanoma cells and to partially purified melanoma-assocd. antigens were coupled to **protein** A-bearing Staphylococcus aureus or **protein** A-Sepharose and used as immunoadsorbents for the indirect immunopptn. of intrinsically radiolabeled **proteins** released into culture medium from various cultured human tumor and nontumor cell lines. These radiolabeled

immunoppts. when analyzed by **SDS-polyacrylamide gel electrophoresis** revealed highly reproducible mol. profiles of **proteins** and glycoproteins released by various cultured tumor lines and control cells into their spent culture media. A comparison of mol. profiles together with data indicating the binding specificity of known xenoantisera produced against human melanoma cells or their exts. led to the discovery of 2 macromols. that are assocd. with human melanoma cells: a glycoprotein with a subunit **mol. wt.** of 240,000 (240K) and a single-chain glycoprotein of 94,000 **daltons** also found in assocn. with human carcinoma cells.

L45 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1980:547890 HCAPLUS
DOCUMENT NUMBER: 93:147890
TITLE: Detection and characterization of **tumor-associated antigenic** components from cell membranes of a uv-light-induced mouse sarcoma using the MEM-technique
AUTHOR(S): Ristau, E.; Schoen, R.; Schlott, B.; Von Broen, B.
CORPORATE SOURCE: Zentralinst. Molekularbiol., DAW, Berlin-Buch, Ger. Dem. Rep.
SOURCE: Acta Biol. Med. Ger. (1980), 39(2-3), 315-25
CODEN: ABMGAJ; ISSN: 0001-5318
DOCUMENT TYPE: Journal
LANGUAGE: German
AB By means of the macrophage electrophoretic mobility (MEM) test on subcellular fractions of the title sarcoma (UVT 15264/Bln), a tumor-assocd. antigen activity was found in the cell membrane fraction. Extn. of this fraction with 2% Triton X-100 or 5% Na cholate gave very heterogeneous **protein** exts., whereas extn. with 3M KCl selectively extd. 3 membrane components: a high-**mol.-wt.** (.apprx.200,000) glycoprotein and 2 low-**mol.-wt.**, carbohydrate-free **proteins**. Removal of the KCl in the presence of Triton X-100 pptd. the latter 2 **proteins**, whereas the glycoprotein preferentially remained in soln. After purifn. of the components in the KCl ext. by preparative **SDS-polyacrylamide gel electrophoresis**, the MEM test showed that only the glycoprotein possessed antigenic activity.

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S2          4   RD (unique items)
?t s2/3 ab/1-4

 2/AB/1     (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI
(c) 2001 Derwent Info Ltd. All rts. reserv.

013844572
WPI Acc No: 2001-328785/200134
XRAM Acc No: C01-100875
 Enhancing immune recognition, useful for protecting or treating an
 individual against malignancies (e.g. leukemia) or infections, by
 administering modified tumor cells that express interferon consensus
 sequence binding protein
Patent Assignee: WHITEHEAD INST BIOMEDICAL RES (WHED  )
Inventor: DALEY G Q; DENG M
Number of Countries: 021  Number of Patents: 001
Patent Family:
Patent No     Kind   Date    Applicat No    Kind   Date     Week
WO 200132843   A2  20010510  WO 2000US41743  A   20001101  200134  B

Priority Applications (No Type Date): US 99163167 A 19991102
Patent Details:
Patent No  Kind Lan Pg   Main IPC    Filing Notes
WO 200132843  A2 E  42 C12N-005/08
   Designated States (National): CA JP
   Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU
   MC NL PT SE TR

Abstract (Basic): WO 200132843 A2
Abstract (Basic):
        NOVELTY - Enhancing immune recognition of cells present in an
    individual and which cause a disease in the individual, comprises
    introducing into the individual modified cells (referred to as
    ICSBP-expressing cells) that express interferon consensus sequence
    binding protein (ICSBP) at a sufficient level to stimulate an immune
    response to the disease-causing cells in the individual.
        DETAILED DESCRIPTION - Enhancing immune recognition of cells
    present in an individual and which cause a disease in the individual,
    comprises introducing into the individual modified cells (referred to
    as ICSBP-expressing cells) that express interferon consensus sequence
    binding protein (ICSBP) at a sufficient level to stimulate an immune
    response to the disease-causing cells in the individual. The immune
    response is greater than the immune response that occurs if
    ICSBP-expressing cells are not introduced into the individual to
    enhance immune recognition of the disease-causing cells. INDEPENDENT
    CLAIMS are also included for the following:
        (1) a method of increasing the immunostimulatory effect of a cell
    comprising enhancing ICSBP expression in the cell;
        (2) a tumor cell, referred to as a modified tumor cell, which is
    replication- or proliferation-incompetent and expresses ICSBP encoded
    by exogenous DNA;
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(3) a method of treating a mammal in whom tumor cells are present, comprising co-administering to the mammal at least one chemotherapeutic agent and the modified tumor cells that express ICSBP from exogenous DNA;

(4) an in vitro method of producing tumor-directed cytotoxic T cell clones comprising:

(a) combining T cells obtained from a mammal, appropriate growth factors and target cells that express ICSBP and against which cytotoxic T-cell clones are to be produced, therefore producing a combination; and

(b) maintaining the combination under conditions appropriate for T cell activation and proliferation, therefore producing cytotoxic T-cells clones directed against the target cells;

(5) a method of producing a mammalian cell that expresses ICSBP comprising activating a gene that encodes ICSBP, where the gene is a silent gene that is not normally expressed in the mammalian cell;

(6) a genetically engineered mammalian cell that expresses ICSBP from a normally silent, activated endogenous gene; and

(7) a method of enhancing the ability of an individual to eliminate cells that cause a condition in the individual, comprising increasing ICSBP levels in the individual to a level which results in elimination of the cells to a greater extent than would occur if ICSBP levels were not increased in the individual.

ACTIVITY - Cytostatic; antimicrobial; immunosuppressive.

To test whether ICSBP-induced immunity could eradicate pre-existing disease, 106 Ba-P210 cells were first injected into naive Balb/c mice to induce leukemia. A single dose of 106 Ba-P210-ICSBP cells were injected simultaneously into the same hosts or following a delaying of 3, 7 or 14 days. Simultaneous injection of both cell lines allowed survival of all mice. When leukemia was allowed to develop for 14 days, equivalent to 2 out of 3 of the disease latency, all mice achieved prolonged survival and 20% of the mice survived disease free. These results demonstrated that the anti-leukemic effect of the immunized cells could be initiated rapidly, and that ectopic ICSBP expression in leukemic cells was potent enough to eradicate established disease.

MECHANISM OF ACTION - Vaccine.

USE - The ICSBP-expressing cells are useful for protecting or treating an individual against malignancies, infections or autoimmune conditions. In particular, the method is useful for enhancing an individual's ability to eliminate cells that cause a disorder, e.g. tumor cells (e.g. chronic myeloid leukemia cells or solid tumor cells) or cell infected with a pathogen (e.g. a virus, a bacterium, a mycobacterium, a parasite, a yeast or a protozoan).

pp; 42 DwgNo 0/6

2/AB/2 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

013565690
WPI Acc No: 2001-049897/200106
XRAM Acc No: C01-013723
Stimulating a systemic antitumor immune response, useful for treatment or prevention, by administering tumor cells modified to express granulocyte-macrophage colony-stimulating factor
Patent Assignee: CELL GENESYS INC (CELL-N)
Inventor: DRANOFF G; HARDY S
Number of Countries: 092 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week

WO 200072686 A1 20001207 WO 2000US15190 A 20000602 200106 B
AU 200054585 A 20001218 AU 200054585 A 20000602 200118

Priority Applications (No Type Date): US 99324707 A 19990602
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200072686 A1 E 109 A01N-063/00
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
AU 200054585 A A01N-063/00 Based on patent WO 200072686

Abstract (Basic): WO 200072686 A1
Abstract (Basic):

NOVELTY - Stimulating a systemic immune response to a tumor, or its antigen (Ag), in a mammal, comprising administering a proliferation-incompetent tumor cell (A) genetically modified to express granulocyte-macrophage colony-stimulating factor (GM-CSF), is new.

DETAILED DESCRIPTION - Stimulating a systemic immune response to a tumor, or its antigen (Ag), in a mammal, comprising administering a proliferation -incompetent tumor cell (A) genetically modified to express granulocyte-macrophage colony-stimulating factor (GM-CSF), is new. (A) is the same type as the tumor being treated, expresses Ag and is modified using a recombinant virus (RV), i.e. adeno, lenti, adeno-associated, SV40, herpes or vaccinia virus, containing the GM-CSF sequence.

INDEPENDENT CLAIMS are also included for the following:

(1) RV;

(2) (A) transformed with RV and able to express GM-CSF; and

(3) kits for stimulating a systemic immune response to tumor or Ag in a mammal comprising RV and a container for holding a (portion of) tumor tissue.

ACTIVITY - Cytostatic.

B16 melanoma cells were transformed to express GM-CSF and interleukin-2, then used for subcutaneous immunization of mice. The animals were challenged with normal B16 cells and 6 of 10 did not develop tumors. When the implanted cells also expressed interleukin-4, 9 of 10 test animals remained free of tumor.

MECHANISM OF ACTION - Stimulation of specific systemic immune response; vaccine.

USE - The method is used to inhibit formation of tumors, and to cause regression, or retard growth, of pre-existing tumors. Non-small cell lung cancer cells were isolated from patients, transformed with a replication-deficient adenovirus that expressed human GM-CSF, irradiated and then used to inoculate the donors, several times at 7-14 day intervals and at doses of 1-10 million cells, intradermally. Development of a delayed hypersensitivity reaction provided evidence for an antitumor response and one patient showed a 50 % reduction in lung and lymph node metastases. Two patients (for whom the inoculating cells were obtained by resection of isolated metastases) remained free of disease for 9-10 months and two other patients for 3 months.

pp; 109 DwgNo 0/19

2/AB/3 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

013193879
WPI Acc No: 2000-365752/200031
XRAM Acc No: C00-110573
XRPX Acc No: N00-273655
Treating and diagnosing cancer comprises contacting serum samples obtained before and after vaccine treatment with an array of proteins from a biological sample
Patent Assignee: CELL GENESYS INC (CELL-N)
Inventor: ANDO D; CHANG J; MCARTHUR J; ROBERTS M; SIMONS J
Number of Countries: 080 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200026676	A1	20000511	WO 99US25936	A	19991103	200031	B
AU 200013409	A	20000522	AU 200013409	A	19991103	200040	

Priority Applications (No Type Date): US 98106795 A 19981103
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200026676	A1	E	92	G01N-033/68	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200013409	A		G01N-033/68	Based on patent WO 200026676

Abstract (Basic): WO 200026676 A1
Abstract (Basic):
NOVELTY - A method for obtaining a tumor-associated antigen (TAA) is new.
DETAILED DESCRIPTION - The method comprises;
(a) preparing an array of proteins from a biological sample;
(b) obtaining a first and second serum sample from a subject before and after, respectively, treatment with a vaccine comprising proliferation incompetent tumor cells expressing GM-CSF and the TAA;
(c) contacting a first sample of the proteins in (a) with the first serum sample;
(d) contacting a second sample of the proteins in (a) with the second serum sample; and
(e) identifying a protein in the array that reacts with the second serum sample but not the first.
INDEPENDENT CLAIMS are also included for the following;
(1) screening for the presence of a TAA comprising;
(a) isolating the TAA identified in the method above;
(b) preparing an antibody against TAA;
(c) contacting the biological specimen with the antibody in (b); and
(d) detecting the presence of an antigen-antibody complex.
(2) a kit for screening the presence of a TAA in a biological sample comprising;
(a) unlabelled first antibodies against a TAA reactive with serum from an individual treated with a vaccine comprising proliferation incompetent tumor cells expressing the TAA and GM-CSF, but not reactive with a pre-treatment serum sample;
(b) a solid support for adhering the biological sample; and
(c) labelled second antibodies against the first antibodies.
ACTIVITY - Cytostatic; antiproliferative.
MECHANISM OF ACTION - The vaccine increases the expression of the tumor associated antigens and enables the identification of tumor cells

by the immune system of the affected individual. No data given.
USE - The method is useful for the identification of tumor-associated antigens.
DESCRIPTION OF DRAWING(S) - The drawing is a schematic representation of the MFG vector containing a cytokine-encoding sequence.
pp; 92 DwgNo 1/18

2/AB/4 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0264186 DBA Accession No.: 2001-03940 PATENT
Stimulating a systemic antitumor immune response, useful for treatment or prevention, by administering tumor cells modified to express granulocyte-macrophage colony-stimulating factor- adeno virus, lenti virus, adeno-associated virus, SV40 virus, herpes virus or vaccinia virus-mediated gene transfer and expression in melanoma cell for cancer recombinant vaccine and gene therapy
AUTHOR: Hardy S; Dranoff G
CORPORATE SOURCE: Foster City, CA, USA.
PATENT ASSIGNEE: Cell-GeneSys 2000
PATENT NUMBER: WO 200072686 PATENT DATE: 20001207 WPI ACCESSION NO.: 2001-049897 (2006)
PRIORITY APPLIC. NO.: US 324707 APPLIC. DATE: 19990602
NATIONAL APPLIC. NO.: WO 2000US15190 APPLIC. DATE: 20000602
LANGUAGE: English
ABSTRACT: A method for stimulating a systemic immune response to a tumor, or its antigen (Ag), in a mammal is new and involves administering a proliferation -incompetent tumor cell (A) genetically modified to express human granulocyte-macrophage colony stimulating factor (GM-CSF), is claimed. (A) is the same type as the tumor being treated, expresses Ag and is modified using a recombinant virus (RV), i.e. adeno virus, lenti virus, adeno-associated virus, SV40 virus, herpes virus or vaccinia virus, containing the GM-CSF sequence. Also claimed are: RV; (A) transformed with RV and able to express GM-CSF; and kits for stimulating a systemic immune response to tumor or antigen in a mammal containing RV and a container for holding a tumor tissue. B16 melanoma cells were transformed to express GM-CSF and interleukin-2, then used for s.c. immunization of mice. The animals were challenged with normal B16 cells and 6 of 10 did not develop tumors. When the implanted cells also expressed interleukin-4, 9 of 10 test animals remained tumor free. The method is useful in inhibiting formation of tumors. (109pp)

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PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
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Set	Items	Description
S1	4	PROLIFERAT?(S)INCOMPETENT(W)(TUMOR? OR TUMOUR?)
S2	4	RD (unique items)

?show files
File 155:MEDLINE(R) 1966-2001/Jul W4
(c) format only 2001 Dialog Corporation
File 5:Biosis Previews(R) 1969-2001/Jul W2
(c) 2001 BIOSIS
File 34:SciSearch(R) Cited Ref Sci 1990-2001/Jul W3
(c) 2001 Inst for Sci Info
File 71:ELSEVIER BIOBASE 1994-2001/Jul W2
(c) 2001 Elsevier Science B.V.
File 73:EMBASE 1974-2001/Jul W2

?ds

Set	Items	Description
S1	167	(GM(W)CSF OR GRANULOCYTE(W)MACROPHAGE?(W)COLONY(W)STIMULATING(W)(FACTOR? OR ACTIVIT?) OR MACROPHAGE(W)GRANULOCYTE(W)CSF) (S)((TUMOR OR TUMOUR OR CANCER?)(W)ASSOCIATED(W)(ANTIGEN OR AG? ?))
S2	56	RD (unique items)
S3	26	S2 AND VACCIN?

?t s3/3 ab/1-26

3/AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11326094 21248499 PMID: 11350882
The influence of granulocyte macrophage colony-stimulating factor and prior chemotherapy on the immunological response to a vaccine (ALVAC-CEA B7.1) in patients with metastatic carcinoma.
von Mehren M; Arlen P; Gulley J; Rogatko A; Cooper HS; Meropol NJ; Alpaugh RK; Davey M; McLaughlin S; Beard MT; Tsang KY; Schlom J; Weiner LM
Department of Medical Oncology, Fox Chase Cancer Center, Philadelphia, Pennsylvania 19111, USA. m vonmehren@fccc.edu
Clinical cancer research (United States) May 2001, 7 (5) p1181-91, ISSN 1078-0432 Journal Code: C2H
Contract/Grant No.: K12 CA01728, CA, NCI; P30 P0 CA06927, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
Granulocyte macrophage colony -stimulating factor (GM -CSF) has been shown to be an effective vaccine adjuvant because it enhances antigen processing and presentation by dendritic cells. ALVAC-CEA B7.1 is a canarypox virus encoding the gene for the tumor -associated antigen carcinoembryonic antigen (CEA) and for a T-cell costimulatory molecule, B7.1. After an initial dose escalation phase, this study evaluated vaccination with 4.5 x 10(8) plaque-forming units ALVAC-CEA B7.1 alone (n = 30) or with GM -CSF (n = 30) in patients with advanced CEA-expressing tumors to determine whether the addition of the adjuvant GM -CSF enhances induction of CEA-specific T-cells. Patients were vaccinated with vaccine intradermally every other week for 8 weeks. GM -CSF was

given s.c. for 5 days beginning 2 days before vaccination . Patients with stable or responding disease after four immunizations received monthly boost injections alone or with GM -CSF . Biopsies of vaccine sites were obtained 48 h after vaccination to evaluate leukocytic infiltration and CEA expression. Induction of peripheral blood CEA-specific T-cell precursors was assessed in HLA-A2 positive patients by an ELISPOT assay looking for the production of IFN-gamma. Therapy was well tolerated. All of the patients had evidence of leukocytic infiltration and CEA expression in vaccine biopsy sites. In the patients receiving GM -CSF , leukocytic infiltrates were greater in cell number but were less likely to have a predominant lymphocytic infiltrate compared with patients receiving vaccine in the absence of the cytokine adjuvant. After four vaccinations , CEA-specific T-cell precursors were statistically increased in HLA-A2 positive patients who received vaccine alone. However, the GM -CSF plus vaccine cohort of HLA-A2 positive did not demonstrate a statistically significant increase in their CEA-specific T-cell precursor frequencies compared with baseline results. The number of prior chemotherapy regimens was negatively correlated with the generation of a T-cell response, whereas there was a positive correlation between the number of months from the last chemotherapy regimen and the T-cell response. ALVAC-CEA B7.1 is safe in patients with advanced, recurrent adenocarcinomas that express CEA, is associated with the induction of a CEA-specific T-cell response in patients treated with vaccine alone but not with vaccine and GM -CSF , and can lead to disease stabilization for up to 13 months.

3/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10806906 99358307 PMID: 10429676
Dendritic cells infiltrating tumors cotransduced with granulocyte/macrophage colony-stimulating factor (GM-CSF) and CD40 ligand genes take up and present endogenous tumor-associated antigens, and prime naive mice for a cytotoxic T lymphocyte response.

Chiodoni C; Paglia P; Stoppacciaro A; Rodolfo M; Parenza M; Colombo MP
Department of Experimental Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy.

Journal of experimental medicine (UNITED STATES) Jul 5 1999, 190 (1) p125-33, ISSN 0022-1007 Journal Code: I2V
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

We transduced BALB/c-derived C-26 colon carcinoma cells with granulocyte / macrophage colony -stimulating factor (GM -CSF) and CD40 ligand (CD40L) genes to favor interaction of these cells with host dendritic cells (DCs) and, therefore, cross-priming. Cotransduced cells showed reduced tumorigenicity, and tumor take was followed by regression in some mice. In vivo tumors were heavily infiltrated with DCs that were isolated, phenotyped, and tested in vitro for stimulation of tumor-specific cytotoxic T lymphocytes (CTLs). BALB/c C-26 carcinoma cells express the endogenous murine leukemia virus (MuLV) env gene as a tumor -associated antigen . This antigen is shared among solid tumors of BALB/c and C57BL/6 mice and contains two epitopes, AH-1 and KSP, recognized in the context of major histocompatibility complex class I molecules H-2Ld and H-2K(b), respectively. DCs isolated from C-26/GM/CD40L tumors grown in (BALB/c x C57BL/6)F1 mice (H-2d x b) stimulated interferon gamma production by both anti-AH-1 and KSP CTLs, whereas tumor-infiltrating DCs (TIDCs) of BALB/c mice stimulated only anti-AH-1 CTLs. Furthermore, TIDCs primed naive mice for CTL activity as early as 2 d after injection into the footpad, whereas

double-transduced tumor cells required at least 5 d for priming; this difference may reflect direct DC priming versus indirect tumor cell priming. Immunohistochemical staining indicated colocalization of DCs and apoptotic bodies in the tumors. These data indicate that DCs infiltrating tumors that produce GM -CSF and CD40L can capture cellular antigens, likely through uptake of apoptotic bodies, and mature in situ to a stage suitable for antigen presentation. Thus, tumor cell-based vaccines engineered to favor the interaction with host DCs can be considered.

3/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10753390 98357448 PMID: 9694075
Transgene expression in dendritic cells to induce antigen-specific cytotoxic T cells in healthy donors.
Philip R; Brunette E; Ashton J; Alters S; Gadea J; Sorich M; Yau J; O'Donoghue G; Lebkowski J; Okarma T; Philip M
RPR Gencell, Santa Clara, California 95054, USA. ramila.philip@rp-rorer.com
Cancer gene therapy (UNITED STATES) Jul-Aug 1998, 5 (4) p236-46, ISSN 0929-1903 Journal Code: CE3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Immunization with specific tumor - associated antigen (Ag) (TAA)-pulsed dendritic cells (DC) has proven to be efficacious in a variety of animal models and is being investigated for the treatment of cancer patients. Use of DC pulsed with specific peptides or transfected with TAA genes has been a focused area of investigation for the induction of potent tumor and viral immune responses. In this study we demonstrate transgene expression, including expression of the MART-1 gene, in DC transfected with plasmid DNA and cationic liposome complexes. These transiently transfected DC, derived from healthy donor monocytes cultured with granulocyte macrophage colony -stimulating factor and interleukin-4, express the transgene and can stimulate naive CD8+ T cells to elicit an antitumor immune response. These cytotoxic T lymphocytes (CTL) were capable of recognizing both known and unknown TAA epitopes and were able to exhibit cytolytic activity against human histocompatibility leukocyte Ag-matched tumor cells expressing the Ag. In addition to their cytolytic function, the CTL displayed an oligoclonal T-cell receptor repertoire, indicating that the presented Ag induced alterations in the T-cell population. The ability to induce tumor-specific CTL in vitro using gene-modified DC transiently expressing TAAs demonstrates the potential use of these Ag-presenting cells to generate future in vivo cancer vaccine strategies.

3/AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10608269 20252784 PMID: 10792287
Vaccination of multiple myeloma patients with idiotype-pulsed dendritic cells: immunological and clinical aspects.
Titzer S; Christensen O; Manzke O; Tesch H; Wolf J; Emmerich B; Carsten C ; Diehl V; Bohlen H
Department of Internal Medicine I, University of Cologne, Joseph-Stelzmannstr. 9, 50924 Cologne, Germany.
British journal of haematology (ENGLAND) Mar 2000, 108 (4) p805-16, ISSN 0007-1048 Journal Code: AXC

Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Multiple myeloma (MM) is characterized by a clonal proliferation of malignant plasma cells in the bone marrow secreting a monoclonal immunoglobulin (paraprotein) with specific antigenic determinants, the idiotype (Id), which can be regarded as a tumour -associated antigen (TAA). In order to analyse the impact of a dendritic cell (DC)-based vaccine , 11 patients with advanced MM were treated with CD34 stem cell-derived dendritic cells that were pulsed with Id peptides. Subsequently, the patients received three boost immunizations every other week with a combination of Id and granulocyte -macrophage colony - stimulating factor (GM - CSF) (nine patients) or with Id peptide-pulsed dendritic cells again (two patients). The treatment was well tolerated with no side-effects. The present clinical study was a proof of concept analysis of dendritic cell-based vaccines in MM. The capacity of the dendritic cells to activate idiotype-specific T cells was verified by in vitro stimulation experiments before the vaccination therapy. Immunological effects of the Id vaccination were analysed by monitoring changes in anti-idiotype antibody titres and idiotype-specific T-cell activity. After vaccination , three out of 10 analysed patients showed increased anti-idiotype antibody serum titres, indicating the induction of an idiotype-specific humoral immune response. The idiotype-specific T-cell response analysed by ELISpot was increased in four out of 10 analysed patients after vaccination , and one patient had a decreased plasma cell infiltration in the bone marrow. In conclusion, five out of 11 patients showed a biological response after vaccination . Thus, our data indicate that immunotherapy with Id-pulsed DCs in MM patients is feasible and safe. DC generated from CD34+ progenitor cells can serve as a natural adjuvant for the induction of clinically relevant humoral and cellular idiotype-specific immune responses in patients suffering from advanced MM.

3/AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10572582 20151766 PMID: 10687150
Dendritic cells loaded with MART-1 peptide or infected with adenoviral construct are functionally equivalent in the induction of tumor-specific cytotoxic T lymphocyte responses in patients with melanoma.
Philip R; Alters SE; Brunette E; Ashton J; Gadea J; Yau J; Lebkowski J; Philip M
RPR Gencell, Hayward, California, USA.
Journal of immunotherapy (UNITED STATES) Jan 2000, 23 (1) p168-76, Journal Code: CUQ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Immunization with tumor-specific-associated antigen--pulsed dendritic cells has proved to be efficacious in various animal models and is being evaluated for the treatment of cancer in humans. Use of dendritic cells pulsed with specific peptides or transfected with tumor -associated antigen genes has been a focused area of investigation for inducing potent tumor and viral immune responses. In this study, the authors demonstrate transgene expression, including the lacZ and MART-1 genes, in dendritic cells infected with adenoviral constructs. These transiently transduced dendritic cells, derived from melanoma patients' monocytes cultured with granulocyte - macrophage colony -stimulating factor and interleukin-4, express the transgene and can stimulate patients' CD8+ T cells to elicit an antitumor immune response comparable to dendritic cells

loaded with a defined peptide. These cytotoxic T lymphocytes were able to recognize both known and unknown tumor -associated antigen epitopes and exhibited cytolytic activity against HLA-matched tumor cells expressing the antigen. The ability to induce tumor-specific cytotoxic T lymphocytes in vitro using gene-modified dendritic cells that transiently express tumor-associated antigens demonstrates the potential use of these antigen-presenting cells for developing in vivo cancer vaccines .

3/AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10203803 99306687 PMID: 10380019
Construction and characterization of a chimeric fusion protein consisting of an anti-idiotype antibody mimicking a breast cancer- associated antigen and the cytokine GM- CSF.
Tripathi PK; Qin H; Bhattacharya-Chatterjee M; Ceriani RL; Foon KA; Chatterjee SK
Department of Internal Medicine, and The Lucille Parker Markey Cancer Center, University of Kentucky Medical Center, Lexington 40536, USA.
Hybridoma (UNITED STATES) Apr 1999, 18 (2) p193-202, ISSN 0272-457X Journal Code: GFS
Contract/Grant No.: UO-1 CA65748, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Anti-idiotype antibody, 11D10 mimics biologically and antigenically a distinct and specific epitope of the high molecular weight human milk fat globule (HMFG), a cancer -associated antigen present in over 90% of breast tumor samples. To augment the immunogenicity of 11D10 without the aid of a carrier protein or adjuvant, we made a chimeric 11D10-GM -CSF fusion protein for use as a vaccine . An expression plasmid for 11D10 was made by ligation of the DNA sequences of the 11D10 light-chain variable region upstream of the human kappa constant region. The heavy-chain plasmid carrying GM -CSF was made by ligation of the heavy-chain variable region sequences upstream of the human gamma1 constant region CH1 fused to the DNA fragment encoding the mature GM -CSF peptide 3' to the CH3 exon. NS1 plasmacytoma cells were transfected with the light and heavy-chain vectors by electroporation. Fusion protein secreted in the culture medium was purified and was characterized by gel electrophoresis as well as by determination of the biological activity of the fused GM -CSF . In nonreducing SDS-polyacrylamide gels, a single band approximately 200 Kd reacted with anti-human kappa, anti-human lambda1 and anti-GM -CSF antibodies. In reducing polyacrylamide gels, a approximately 74 kd protein reacted with anti-human lambda1 and anti-GM -CSF antibodies. The fusion protein induced proliferation of GM -CSF dependent NFS-60 cells. These results suggest that the protein is a chimeric anti-idiotype antibody consisting of 11D10 variable domains, human kappa and lambda1 constant domains and that the GM -CSF moiety fused to the constant region lambda1 is biologically active.

3/AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09739816 98212731 PMID: 9551367
Autologous human dendriphages pulsed with synthetic or natural tumor peptides elicit tumor-specific CTLs in vitro.
Tjandrawan T; Martin DM; Maeurer MJ; Castelli C; Lotze MT; Storkus WJ

Department of Pathology, University of Pittsburgh School of Medicine, Pennsylvania 15261, USA.
Journal of immunotherapy (UNITED STATES) Mar 1998, 21 (2) p149-57, Journal Code: CUQ
Contract/Grant No.: CA 57840, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The recent identification of tumor-associated antigens and tumor - associated antigen -derived peptide epitopes recognized by cytolytic T lymphocytes (CTLs) in the context of major histocompatibility complex (MHC) class I molecules has prompted the development of peptide-based vaccines for the treatment of human cancers, particularly melanoma. The design of such clinical protocols requires an understanding of the inherent immunogenicity of the peptide(s) and a choice of a facilitating adjuvant promoting cellular immunity against these peptides. We have evaluated the abilities of a series of defined synthetic peptide epitopes derived from MART-1/Melan-A, gp100, tyrosinase, and MAGE-3 or unfractionated peptides naturally presented by melanoma MHC molecules to elicit HLA-A2-restricted and melanoma-reactive CTLs from the peripheral blood of normal donors or patients with metastatic melanoma. Autologous peripheral blood dendritic cells (DCs), which were easily generated from all donors when cultured in the presence of recombinant human interleukin-4 and recombinant human granulocyte -macrophage colony -stimulating factor were pulsed with melanoma peptides and used to "prime" and/or "boost" CTL cultures in vitro. Our results suggest that antimelanoma CTLs may be reproducibly generated in short-term in vitro cultures in this manner using either a subset of the defined synthetic peptides (MART-1/Melan-A27-35, MART-1/Melan-A32-40, gp100(280-288), tyrosinase368-376, and MAGE-3(271-279)) or unfractionated peptides (containing both idiotypic and shared melanoma epitopes) derived from freshly isolated autologous melanoma lesions. These in vitro data support the use of autologous DCs prepulsed with such peptides as an appropriate antigen adjuvant delivery system in melanoma peptide-based vaccines .

3/AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06829963 92203854 PMID: 1803182
Chemotherapy and immunotherapy of colorectal cancer.
Masucci G; Ragnhammar P; Frodin JE; Hjelm AL; Wersall P; Fagerberg J; Osterborg A; Mellstedt H
Department of Oncology (Radiumhemmet), Karolinska Hospital, Stockholm, Sweden.
Medical oncology and tumor pharmacotherapy (ENGLAND) 1991, 8 (3) p207-20, ISSN 0736-0118 Journal Code: LSP
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
More than 50% of the patients with large bowel cancer develop disseminated disease and invariably succumb. Adjuvant chemotherapy with 5-FU and levamisole have been shown to be more efficient than 5-FU alone or in combination with cytostatics. The combination of 5-FU, leukovorin and methotrexate induces prolonged survival with a good quality of life in metastatic colorectal cancer (CRC). During the last decade tumor immunotherapy has been an alternative facilitated by isolation and large scale production of cytokines and monoclonal antibodies. The mouse monoclonal antibody (MAb) 17-1A recognizes a tumor -associated antigen (TAA), present in high concentrations on the surface of gastrointestinal

tumor cells. Injections of MAb 17-1A in patients with metastatic CRC induced generation of anti-idiotypic (ab2) in 90% and anti-anti-idiotypic (ab3) antibodies in 47% of the treated patients. The development of ab3 correlated significantly with survival (mean 80 weeks) while ab3- patients survive only 38 weeks. One of 52 patients treated with MAb 17-1A is a complete remission after 66 months, 3 had minor regression and 6 had a stable disease (19% RR). Based on in vitro findings showing increased antibody-dependent cellular cytotoxicity (ADCC) by the combination of granulocyte -macrophage colony stimulating factor (GM -CSF) and MAb 17-1A, 16 CRC patients have been treated with subcutaneously injections of GM -CSF for 10 days and intravenous infusions of MAb 17-1A at day 3. Two of 16 are in CR, 1 in MR and 3 in SD (37.5% RR). Minor side-effects were registered. A further development of immunotherapy of CRC might imply vaccination by injection of specific human anti-idiotypic antibodies (ab2) which mimics the nominal antigen, in order to induce a specific immunity.

3/AB/9 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12974389 BIOSIS NO.: 200100181538
Enhancement of B cell lymphoma and tumor resistance using idiotype/cytokine conjugates.
AUTHOR: Levy Ronald(a); Tao Mi-Hua
AUTHOR ADDRESS: (a)Stanford, CA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1237 (2):pNo Pagination Aug. 8, 2000
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: B cell lymphoma tumor -associated antigen or a fragment thereof containing an epitope are linked to an immune-enhancing cytokine, such as GM -CSF , IL-2, or IL-4 to form an immuno-complex. This immuno-complex elicits immune responses which are protective with respect to tumor proliferation. The linkers may be simple chemical bifunctional moieties introduced through chemical synthetic techniques or peptides introduce through recombinant methodologies. Antibodies immunoreactive with these immunocomplexes are also useful as passive vaccines and as analytical tools.

2000

3/AB/10 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12146520 BIOSIS NO.: 199900441369
Inhibition of implanted tumor growth in nude mice by way of inducing apoptosis by immune response induced by dendritic cells pulsed with tumor extracts in vivo.
AUTHOR: Li Mingsong(a); Yuan Aili(a); Tan Xiaohua(a)
AUTHOR ADDRESS: (a)Department of Gastroenterology, Nanfang Hospital, First Military Medical University, Guangzhou**China
JOURNAL: Zhongguo Zhongliu Linchuang 26 (3):p222-224 Feb., 1999
ISSN: 1000-8179

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Chinese; Non-English
SUMMARY LANGUAGE: Chinese; English

ABSTRACT: Objective: To study the mechanism of antitumor immune response induced by dendritic cells (DC) in the inhibition of growth of implanted tumor in nude mice by way of inducing tumor cell apoptosis. Methods: Isolated and purified DC derived from hepatocellular cancer (HCC) patients with granulocyte /macrophage colony stimulating factor and interleukin 4; extracted tumor -associated antigen (TAA) from human hepatocellular cancer cell line HepG2 tumor cells; Stimulated T lymphocytes with DC pulsed by TAA to produce CTL (cytotoxic T lymphocyte); Implanted the CTL to inhibit the growth of implanted tumor in nude mice; Evaluated the apoptosis of tumor cells. Results: The DC from HCC patients pulsed with TAA from HepG2 tumor cells could stimulate T lymphocyte immune response inhibiting the growth of implanted tumor in nude mice by way of inducing tumor cell apoptosis. Conclusion: As a new concept anti-tumor vaccine of DC pulsed by TAA may play an important role in therapy of tumor.

1999

3/AB/11 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09701928 Genuine Article#: 438KA Number of References: 72
Title: Synergy of vaccine strategies to amplify antigen-specific immune responses and antitumor effects (ABSTRACT AVAILABLE)
Author(s): Grosenbach DW; Barrientos JC; Schlom J (REPRINT) ; Hodge JW
Corporate Source: NCI,Tumor Immunol & Biol Lab, NIH,10 Ctr Dr,Room 8B09/Bethesda//MD/20892 (REPRINT); NCI,Tumor Immunol & Biol Lab, NIH,Bethesda//MD/20892; NIH,Howard Hughes Med Inst,Bethesda//MD/20892
Journal: CANCER RESEARCH, 2001, V61, N11 (JUN 1), P4497-4505
ISSN: 0008-5472 Publication date: 20010601
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA
Language: English Document Type: ARTICLE
Abstract: Several different vaccine strategies have been evaluated and combined in an attempt to amplify T-cell responses toward induction of antitumor immunity. The model tumor antigen used was carcinoembryonic antigen (CEA), While initial T-cell activation studies were conducted in conventional mice, combined vaccine strategy studies and antitumor studies were conducted in transgenic mice in which CEA is expressed in normal gastrointestinal tissue and CEA protein is found in sera. The studies reported here demonstrate: (a) A recombinant avipox (fowlpox, rF) vector expressing the signal 1 (CEA) and the B7-1 costimulatory molecule transgenes (designated rF-CEA/B7-1) is more potent in inducing CEA-specific T-cell responses than rF-CEA; one administration of recombinant fowlpox vector expressing CEA and three different costimulatory molecule transgenes (B7-1, ICAM-1, LFA-3, designated rF-CEA/TRICOM) was more potent in inducing CEA-specific T-cell responses than four vaccinations with rF-CEA or two vaccinations with rF-CEA/B7-1, Moreover, up to four vaccinations with rF-CEA/TRICOM induced greater CEA-specific T-cell responses with each vaccination . (b) A diversified prime and boost strategy using a prime with a recombinant vaccinia vector expressing CEA and the triad of costimulatory molecules (designated rV-CEA/TRICOM) and a boost with rP-CEA/TRICOM was more potent in inducing CEA-specific T-cell responses

than the repeated use of rF-CEA/TRICOM alone. (c) The addition of granulocyte macrophage colony-stimulating factor (GM-CSF) to the rF-CEA or rF-CEA/TRICOM vaccinations via the simultaneous administration of a rF-GM-CSF vector enhanced CEA-specific T-cell responses, These strategics (TRICOM/diversified prime and boost/GM-CSF) were combined to treat CEA-expressing carcinoma Liver metastases in CEA-transgenic mice; vaccination was initiated 14 days posttumor transplant. Antitumor effects in terms of survival and CD8(+) and CD4(+) responses specific for CEA were also observed in this CEA-transgenic mouse model. These studies demonstrate that the use of cytokines and diversified prime and boost regimens can be combined with the use of recombinant vectors expressing signal 1 and multiple costimulatory molecules to further amplify T-cell responses toward more effective vaccine strategies.

3/AB/12 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08760303 Genuine Article#: 326LN Number of References: 13
Title: Ex vivo gene therapy using granulocyte-macrophage colony-stimulating factor-transduced tumor vaccines (ABSTRACT AVAILABLE)
Author(s): Kawai K (REPRINT) ; Tani K; Asano S; Akaza H
Corporate Source: UNIV TSUKUBA,INST CLIN MED, DEPT UROL, 1-1-1 TENNODAI/TSUKUBA/IBARAKI 305/JAPAN/ (REPRINT); UNIV TOKYO,INST MED SCI, DEPT MED ONCOL/TOKYO//JAPAN/
Journal: MOLECULAR UROLOGY, 2000, V4, N2 (SUM), P43-46
ISSN: 1091-5362 Publication date: 20000600
Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538
Language: English Document Type: ARTICLE
Abstract: There is no standard effective therapy for metastatic renal-cell carcinoma (RCC) or prostate cancer. Both of these cancers may be immunogenic, so therapy targeted to a tumor -associated antigen may be effective. Transduction of the gene encoding granulocyte - macrophage colony -stimulating factor has shown promise in preclinical studies, and clinical trials are in their early stages. Both autologous cancer cells and partially HLA-matched allogenic cells are being studied. No dose-limiting side effects have been observed, and a few patients have had transient objective tumor regressions. Further trials with more frequent and, probably, longer immunization schedules are needed to define efficacy.

3/AB/13 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

01758701 2001120296
Three different vaccines based on the 140-amino acid MUC1 peptide with seven tandemly repeated tumor-specific epitopes elicit distinct immune effector mechanisms in wild-type versus MUC1-transgenic mice with different potential for tumor rejection
Soares M.M.; Mehta V.; Finn O.J.
ADDRESS: Dr. O.J. Finn, Department of Molecular Genetics, W1142 Biomedical Science Tower, University of Pittsburgh, Pittsburgh, PA 15261, United States
EMAIL: ojfinn@pitt.edu
Journal: Journal of Immunology, 166/11 (6555-6563), 2001, United States
PUBLICATION DATE: May 1, 2001
CODEN: JOIMA
ISSN: 0022-1767

DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 75

Low-frequency CTL and low-titer IgM responses against tumor -associated Ag MUC1 are present in cancer patients but do not prevent cancer growth. Boosting MUC1-specific immunity with vaccines , especially effector mechanisms responsible for tumor rejection, is an important goal. We studied immunogenicity, tumor rejection potential, and safety of three vaccines : 1) MUC1 peptide admixed with murine GM -CSF as an adjuvant; 2) MUC1 peptide admixed with adjuvant SB-AS2; and 3) MUC1 peptide-pulsed dendritic cells (DC). We examined the qualitative and quantitative differences in humoral and T cell-mediated MUC1-specific immunity elicited in human MUC1-transgenic (Tg) mice compared with wild-type (WT) mice. Adjuvant-based vaccines induced MUC1-specific Abs but failed to stimulate MUC1-specific T cells. MUC1 peptide with GM -CSF induced IgG1 and IgG2b in WT mice but only IgM in MUC1-Tg mice. MUC1 peptide with SB-AS2 induced high-titer IgG1, IgG2b, and IgG3 Abs in both WT and MUC1-Tg mice. Induction of IgG responses was T cell independent and did not have any effect on tumor growth. MUC1 peptide-loaded DC induced only T cell immunity. If injected together with soluble peptide, the DC vaccine also triggered Ab production. Importantly, the DC vaccine elicited tumor rejection responses in both WT and MUC1-Tg mice. These responses correlated with the induction of MUC1-specific CD4SUP+ and CD8SUP+ T cells in WT mice, but only CD8SUP+ T cells in MUC1-Tg mice. Even though MUC1-specific CD4SUP+ T cell tolerance was not broken, the capacity of MUC1-Tg mice to reject tumor was not compromised.

3/AB/14 (Item 1 from file: 77)
DIALOG(R)File 77:Conference Papers Index

4579156
Supplier Accession Number: 01-03431 V29N03
Gene gun-mediated DNA vaccination with idiotype/granulocyte - Macrophage colony-stimulating factor fusion gene induces antibody responses against the tumor associated antigen, EpCAM in EpCAM-transgenic mice
Mosolits, S.; Campbell, F.; Litvinov, S.V.; Fagerberg, J.; Crowe, J.S.; Mellstedt, H.; Ellis, J.H.
Karolinksa Inst., Stockholm, Sweden
Human Antibodies and Hybridomas 0005434 Prague (Czech Republic) 23-25 Apr 2001
The International Journal of Human Antibodies, Smith Kline Beecham, Bioinvent, Celltech, Abgenix
Meetings Management, Station Lane, Milford, Surrey, GU8 5AD, UK; phone: 44 (0)1483 427770; fax: 44 (0)1483 428516; URL: http://www.meetingsmanagement.com

3/AB/15 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01705258 SUPPLIER NUMBER: 19614961 (USE FORMAT 7 OR 9 FOR FULL TEXT)
GM-CSF transduced tumor cells effective against brain tumors.
Marble, Michelle
Cancer Weekly Plus, p10(2)
July 14,
1997
PUBLICATION FORMAT: Newsletter LANGUAGE: English RECORD TYPE: Fulltext

TARGET AUDIENCE: Professional
WORD COUNT: 727 LINE COUNT: 00067

3/AB/16 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01667370 SUPPLIER NUMBER: 19012170 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Immunotherapeutic approaches to the elimination of minimal residual disease.(Research from Conferences)
Baynes, R.D.; Heitz-Turner, T.; Wood, G.W.
Cancer Weekly Plus, p18(2)
Dec 23,
1996
PUBLICATION FORMAT: Newsletter LANGUAGE: English RECORD TYPE: Fulltext
TARGET AUDIENCE: Professional
WORD COUNT: 444 LINE COUNT: 00040

3/AB/17 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

013628257
WPI Acc No: 2001-112465/200112
XRAM Acc No: C01-033494
XRPX Acc No: N01-082531
Diagnosing a disorder characterized by expression of a human cancer associated antigen precursor, comprises detecting interaction of an agent with a nucleic acid molecule encoding the antigen precursor
Patent Assignee: LUDWIG INST CANCER RES (LUDW-N)
Inventor: PFREUNDSCHUH M; SAHIN U; TURECI O
Number of Countries: 023 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200100874	A2	20010104	WO 2000US17207	A	20000623	200112	B
AU 200056325	A	20010131	AU 200056325	A	20000623	200124	

Priority Applications (No Type Date): US 99346498 A 19990630
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200100874	A2	E	126	C12Q-001/68	

Designated States (National): AU CA CN JP KR
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

AU 200056325	A		C12Q-001/68	Based on patent WO 200100874

Abstract (Basic): WO 200100874 A2
Abstract (Basic):

NOVELTY - Diagnosing a disorder characterized by expression of a human cancer associated antigen (CAA) precursor (I) coded by a NA Group 1 nucleic acid molecule (N1) comprising contacting the biological sample with an agent (A) that specifically binds to N1, (I) or its fragment, complexed with an human leukocyte antigen (HLA) molecule and determining the interaction between the agent and N1 or (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) determining regression, progression or onset of a condition characterized by abnormal expression of a protein encoded by N1, by monitoring a sample from a patient who has or is suspected of having

the condition for:

(a) (a peptide derived from) the protein;

(b) an antibody that selectively binds to the protein or peptide; and

(c) cytotoxic T-lymphocytes (CTL) specific for a complex of the peptide derived from the protein and a major histocompatibility complex (MHC) molecule, as a determination of regression, progression or onset of the condition;

(2) a pharmaceutical preparation (P1) for a human subject comprising (A) which enriches selectively the presence of the complex of human leukocyte antigen (HLA) molecule and CAA, which is a fragment of (I), when administered to the subject;

(3) a composition comprising an isolated agent that binds selectively to a PP Group I polypeptide (I), or its conjugate;

(4) a pharmaceutical composition (P2) comprising an isolated nucleic acid molecule, N1 or NA Group 2 molecules (N2) which are fragments of N1, which code for a polypeptide or its portion which binds an MHC molecule to form a complex recognized by an autologous antibodies or lymphocyte;

(5) a pharmaceutical composition (P3) comprising an isolated polypeptide comprising (I) or a PP Group 2 polypeptide (Ia) encoded by N2;

(6) an isolated nucleic acid molecule (IIa) comprising:

(a) a NA Group 3 molecule (N3) which is the subset of N1 containing previously unknown human nucleic acids coding for (I);

(b) deletions, additions and substitutions which code for (I);

(c) a sequence that differs from the above said nucleic acids due to degeneracy of genetic code, or their complements; or

(d) a NA Group 4 molecule (N4) which codes for a polypeptide which binds to MHC molecule to form a complex recognized by an autologous antibody or lymphocyte;

(7) an isolated nucleic acid molecule (IIb) comprising:

(a) a fragment of a nucleic acid molecule containing S1 of sufficient length to represent a unique sequence within a human genome; or

(b) identified nucleic acid encoding (I) or its complements, such that the fragment includes a sequence of contiguous nucleotides which is not identical to any of the sequences given under the GenBank accession numbers, given in the specification, their complements or fragments;

(8) an expression vector (III) comprising (IIa) or (IIb) operably linked to a promoter;

(9) an expression vector (IIIa) comprising N2 operably linked to a promoter;

(10) an expression vector comprising N1 or N2, and a nucleic acid encoding a HLA molecule;

(11) a host cell (IV) transformed or transfected with (III) or (IIIa), and further comprising a nucleic acid encoding a HLA molecule;

(12) an isolated polypeptide encoded by (IIa);

(13) an immunogenic fragment of the above said polypeptide;

(14) an isolated fragment of (I) or its portion, which binds to HLA on human antibody;

(15) a kit (K) for detecting the presence or expression of (I) by a pair of nucleic acid molecules essentially consisting of contiguous segment of nucleotides 12-32 of N1, or its complements, such that the segments are non-overlapping;

(16) a composition of matter useful in stimulating an immune response to (I), containing a number of peptides derived from amino acid sequences of the proteins, which bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein; and

(17) an isolated antibody which selectively binds to a complex of a peptide derived from (I), and an MHC molecule to which the peptide binds to form the complex, such that the antibody does not bind the peptide or MHC molecule alone.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Gene therapy; vaccine . No supporting data given.

USE - Treating a subject with a condition characterized by expression of (I) in cells of a subject comprising:

(1) removing an immunoreactive cell containing sample from the subject;

(2) contacting the sample to a host cell comprising N1-N4 or NA group 5 molecule (N5) which is a subset of N1 containing CAA that reacts with allogeneic cancer antisera, for production of CTL against CAA, which is fragment of (I); and

(3) introducing CTL to the subject to lyse cells which express CAA; or

(4) identifying a nucleic acid molecule, preferably N1, expressed by the cells associated with the disease condition;

(5) transfecting a host cell with N1, its fragment or its variant;

(6) culturing the transfected cell to express the transfected nucleic acid molecule; and

(7) introducing the host cells or its extract to increase an immune response against the cell of the subject.

Treating, diagnosing or monitoring a subject having a condition characterized by abnormal expression of (I), by:

(1) administering an antibody coupled to a therapeutically useful agent which specifically binds to a protein or the peptide;

(2) administering a pharmaceutical composition to prevent, delay onset of, or inhibit the condition in the subject; or3) identifying cells from the subject which express abnormal amounts of proteins, isolating a sample of cells, cultivating a cell and introducing the cells to provoke an immune response against the cells.

(A) is useful to treat pathological condition or disorder characterized by expression of (I) (all claimed). CAAs, the nucleotides encoding them, antibodies against them and the pharmaceutical compositions comprising them are useful for diagnosing, monitoring and treating the diseases characterized by the expression of one or more CAAs.

pp; 126 DwgNo 0/1

3/AB/18 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

010560750
WPI Acc No: 1996-057704/199606
XRAM Acc No: C96-019148
Breast cancer vaccine, developing lymphocyte immunity - contg. tumour associated antigen and low, non-toxic doses of granulocyte-macrophage colony stimulating factor and interleukin-2
Patent Assignee: ELLIOTT R L (ELLI-I); HEAD J F (HEAD-I)
Inventor: ELLIOTT R L; HEAD J F
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5478556	A	19951226	US 94202516	A	19940228	199606	B

Priority Applications (No Type Date): US 94202516 A 19940228
Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes
US 5478556 A 8 A61K-045/05

Abstract (Basic): US 5478556 A

A compsn. comprises 0.1 ml of a suspension contg. a human breast cancer tumour associated antigen (TAA), 1,000,000 CFU of granulocyte -macrophage colony stimulating factor (GM -CSF) and 10,000 IU of interleukin-2 (IL-2). Also claimed is a breast tumour vaccine comprising a suspension of a TAA from a human breast tumour, 1,000,000 CFU of GM -CSF and 10,000 IU of IL-2, pref. in a vol. of ca. 0.3 ml.

USE - The vaccine is used in a cancer vaccination process, involving priming the patient's immune system with a chemotherapeutic antineoplastic agent (e.g. cisplatin-transferrin) prior to vaccination , to stimulate lymphocyte proliferation; administering the vaccine (pref. intradermally into the groin area, where inguinal and mesentery lymph node drainage promotes infiltration of lymphocytes and monocytes into the injection site; and administering an oral lymphocyte proliferative stimulator (e.g. the antidepressant fluoxetine) simultaneously with and after the vaccination . The developed lymphocyte immunity against TAA is useful in growth control or eradication of occult or evident metastatic cancer cells.

ADVANTAGE - The combination of agents optimises potential development of lymphocyte immunity against tumours. GM-CSF stimulates monocytes (vital in antigen processing and antigen presentation to lymphocytes); and IL-2 stimulates clonal expansion of T-lymphocytes. There are no toxicity problems, since IL-2 and GM-CSF are used at low doses, with only three weekly injections.

Dwg.0/3

3/AB/19 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0223345 DBA Accession No.: 98-04942 PATENT
Immunogenic composition for treating cancer comprises tumor-associated antigen - cytokine-mediated cancer gene therapy
AUTHOR: Hiserodt J C; Graf M R; Granger G A
CORPORATE SOURCE: Oakland, CA, USA.
PATENT ASSIGNEE: Univ.California 1998
PATENT NUMBER: WO 9804282 PATENT DATE: 980205 WPI ACCESSION NO.: 98-130421 (9812)
PRIORITY APPLIC. NO.: US 901225 APPLIC. DATE: 970724
NATIONAL APPLIC. NO.: WO 97US13205 APPLIC. DATE: 970725
LANGUAGE: English
ABSTRACT: An immunogenic composition contains a tumor -associated antigen (Ag) obtained from an autologous cell, preferably a tumor cell, or its progeny, and allogeneic cells, preferably ovary or brain cancer cells, genetically engineered to produce a cytokine, preferably a transmembrane cytokine, at high levels. Alternatively the Ag may be replaced by autologous tumor cells or their progeny. The cytokine is preferably interleukin (IL)-4, granulocyte -macrophage colony stimulating factor , IL-2, tumor necrosis factor, or macrophage colony stimulating factor. The autologous tumor cell is preferably a glioma cell, glioblastoma cell, gliosarcoma cell, astrocytoma cell or ovary cancer cell. The autologous or allogeneic cells may be inactivated. The compositions are used as vaccines to induce an antitumor response, particularly for treating ovary or brain cancer. Particularly they are used after preliminary treatment by surgery, chemotherapy or radiation therapy. The vaccines can be tailored for

specific cancers or subjects. The cytokine provide a better response than tumor cells used alone or with adjuvants. (65pp)

3/AB/20 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0218970 DBA Accession No.: 98-00567 PATENT
Anticancer vaccine containing genetically modified dendritic cells- cancer ex vivo gene therapy by lipofection with a plasmid pCMV/MUC1 vector containing a mucin gene
AUTHOR: Pecher G
CORPORATE SOURCE: Berlin, Germany.
PATENT ASSIGNEE: Pecher G 1997
PATENT NUMBER: DE 19617837 PATENT DATE: 971023 WPI ACCESSION NO.: 97-514604 (9748)
PRIORITY APPLIC. NO.: DE 1017837 APPLIC. DATE: 960419
NATIONAL APPLIC. NO.: DE 1017837 APPLIC. DATE: 960419
LANGUAGE: German
ABSTRACT: A new anti-cancer agent contains autologous human dendritic cells, which have been transfected with a fragment of a human MUC1 gene containing several tandem repeat sequences, and express tumor - associated antigen epitopes, preferably on the cell surface, when treated with a glycosylation-inhibitor. The dendritic cells are transfected with the MUC1 gene fragment using a liposome preparation, optionally using plasmid pCMV/MUC1, containing the MUC1 gene fragment under the control of a cytomegalo virus immediate-early promoter. The MUC1 gene fragment preferably has 12-40 (especially 22) tandem repeat sequences. The glycosylation-inhibitor is preferably phenyl N-acetyl-alpha-D-galactosaminide. The dendrite cells may be CD1a-, CD80- and CD86-expressing cells isolated from peripheral blood of patients or healthy subjects using interleukin-4 and granulocyte - macrophage colony stimulating factor . The recombinant cells may be used in gene therapy of MUC1-expressing tumors, especially mamma, pancreas, ovary, colon or parotid tumors. (6pp)

3/AB/21 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0190742 DBA Accession No.: 96-01513
DNA vaccines against B-cell tumors- genetic immunization with a B-lymphocyte idiotype single chain antibody tumor-associated antigen gene in a plasmid vector (conference abstract)
AUTHOR: Stevenson F K; Zhu D; Hawkins R E; Ashworth L J; Thompsett A; King C A; Spellerberg M B; Kumar S; Hamblin T J
CORPORATE AFFILIATE: Univ.Southampton-Hosp. Med.Res.Counc.
CORPORATE SOURCE: Molecular Immunology Group, Tenovus Laboratory, Southampton University Hospitals, Southampton SO16 6YD, UK.
JOURNAL: Immunology (86, Suppl.1, 7) 1995
ISSN: 0019-2805 CODEN: IMMUAM
CONFERENCE PROCEEDINGS: British and Netherlands Societies for Immunology, Joint Congress, Brighton, UK, 6-8 December, 1995.
LANGUAGE: English
ABSTRACT: DNA vaccines , where tumor antigen is delivered to the host via plasmid DNA, should allow targeting of the encoded antigen to a chosen pathway of the immune system. For B-lymphocyte tumors, the clonal idiotypic Ig synthesized by the tumor cell represents a tumor - associated antigen with potential as a vaccine . This antigen is

composed of variable region sequences of heavy (VH) and light (VL) chains, and differs for each patient. VH and VL genes were isolated from lymphoid tissue and assembled as Fv single chain antibody (scFv) sequences in plasmid vectors, using simple and rapid methods. On injection into mouse muscle, plasmids induced low serum levels of anti-idiotypic antibody. Splenocytes also gave a proliferative response to idiotypic tumor protein. A clinical trial on advanced lymphoma patients was initiated. In mouse models, idiotypic DNA vaccines induced dose-dependent specific protection against lymphoma. Immune responses and protection could be boosted by co-transfection of a vector encoding granulocyte - macrophage colony stimulating factor , whereas an interleukin-2 vector was ineffective. (0 ref)

3/AB/22 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0186957 DBA Accession No.: 95-14472
DNA immunization induces specific antitumor immunity and protects mice against tumor challenge- tumor- associated antigen, granulocyte - macrophage colony stimulating factor and human immunoglobulin constant region DNA for use in genetic immunization (conference abstract)
AUTHOR: Syrengelas A D; Levy R
CORPORATE AFFILIATE: Univ.Stanford
CORPORATE SOURCE: Department of Medicine, Division of Oncology, Stanford University School of Medicine, Stanford, CA 94305, USA.
JOURNAL: FASEB J. (9, 3, A494) 1995
ISSN: 0892-6638 CODEN: FAJOEC
CONFERENCE PROCEEDINGS: Experimental Biology 95, Atlanta, Georgia, 9-13 April, 1995.
LANGUAGE: English
ABSTRACT: The sequence encoding the antigenic determinant contained within the variable regions of the surface immunoglobulin (Ig) of the 38C13 mouse B-lymphocyte lymphoma model was cloned into a plasmid containing the human Ig constant region sequences with or without the mouse granulocyte-macrophage colony stimulating factor (GM-CSF) sequence. Mice received 3 i.m. injections of plasmid at 3 wk intervals. Antibodies against the human constant region were produced in mice injected with these vectors. Furthermore, a specific anti-idiotypic antibody response was observed in mice immunized with DNA containing the 38C13 variable region sequences. Immunization with the GM-CSF fusion construct resulted in earlier anti-idiotypic antibody induction as well as a higher proportion of responsive mice. Immunization with DNA encoding only the tumor Ig resulted in anti-idiotypic antibody induction, whereas immunization with the Ig protein required fusion with GM-CSF for the induction of such a response. Genetic immunization also protected mice against subsequent challenge with a lethal tumor dose. (0 ref)

3/AB/23 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0183393 DBA Accession No.: 95-10214
Applications of antibody gene technology- antibody engineering by phage display technology and use of antibody gene in genetic immunization or cytokine-mediated gene therapy of cancer (conference abstract)
AUTHOR: Hawkins R E

CORPORATE AFFILIATE: Med.Res.Counc. Univ.Cambridge
CORPORATE SOURCE: CRC Department of Clinical Oncology and Cambridge Centre for Protein Engineering, Hills Road, Cambridge CB2 2QH, UK.
JOURNAL: Br.J.Cancer (71, Suppl.24, 1) 1995
ISSN: 0007-0920 CODEN: BJCAAI
CONFERENCE PROCEEDINGS: British Association for Cancer Research (36th Annual Meeting) and Association of Cancer Physicians (10th Annual Meeting), Nottingham, UK, 2-5 April, 1995.
LANGUAGE: English
ABSTRACT: Polymerase chain reaction and sequencing were used to identify genes encoding tumor-derived antibody variable regions (V) (as a tumor - associated antigen and antitumor target) from lymph node biopsies of patients with B-lymphocyte lymphoma. VH and VL genes were identified in 11/13 patients. Plasmid genetic immunization was tested for therapeutic anti-idiotype vaccination . In mice, antibody and T-lymphocyte responses were generated to the idiotypic antigens, and a phase-I clinical trial was initiated. Enhanced immune responses were obtained by incorporating e.g. granulocyte -macrophage colony stimulating factor or interleukin-2 genes into the vectors. Repertoires of V genes and phage display technology were used in construction of large combinatorial libraries (e.g. 10 power 11) of antibody fragments for direct selection. Antibodies from phage display libraries were tested in imaging trials and used in conjugate production. Gene therapy may be used to target delivery and expression of antibody fragments locally within tumors, to enhance specificity and enhance the effectiveness of antibody-based therapy. (0 ref)

3/AB/24 (Item 6 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0177722 DBA Accession No.: 95-04543 PATENT
New recombinant swine-pox virus- vector for antigen, cytokine or cytokine receptor gene cloning and expression for use as a recombinant vaccine
AUTHOR: Cochran M D; Junker D E
PATENT ASSIGNEE: Syntro 1995
PATENT NUMBER: WO 9503070 PATENT DATE: 950202 WPI ACCESSION NO.: 95-075025 (9510)
PRIORITY APPLIC. NO.: US 97554 APPLIC. DATE: 930722
NATIONAL APPLIC. NO.: WO 94US8277 APPLIC. DATE: 940722
LANGUAGE: English
ABSTRACT: A new swine-pox virus recombinant vaccine vector, e.g. S-SPV-031, has a gene and promoter in a non-essential site (e.g. the thymidine-kinase (EC-2.7.1.21) gene). The gene may encode an antigen from human herpes virus, herpes simplex virus-1 or -2, human cytomegalo virus, Epstein-Barr virus, varicella-zoster virus, human herpes virus-6 or -7, horse herpes virus-1 (glycoprotein-B or -D), horse influenza virus (type-A Alaska-91, Prague-56, Miami-63 or Kentucky-81 neuraminidase (NA, EC-3.2.1.18)), human influenza virus, HIV virus, rabies virus, measles virus, hepatitis B virus (core antigen or surface antigen), hepatitis C virus, cattle respiratory-syncytial virus (attachment protein-G, fusion protein-F or nucleocapsid protein-N), cattle parainfluenza virus-3 (fusion protein or hemagglutinin-NA), cattle viral-diarrhea virus (glycoprotein-48 or -53), infectious-bursal-disease virus (polyprotein), Plasmodium falciparum or Bordetella pertussis, a tumor - associated antigen , human interleukin-2, interleukin-6, interleukin-12, interferon, granulocyte -macrophage colony stimulating factor or interleukin receptor. (338pp)

3/AB/25 (Item 7 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0169612 DBA Accession No.: 94-12163 PATENT
Modified recombinant virus- antitumor recombinant vaccine production with vaccinia virus or canary-pox virus vector and tumor necrosis factor, tumor-associated antigen, interleukin, interferon gene, etc.
PATENT ASSIGNEE: Virogenetics 1994
PATENT NUMBER: WO 9416716 PATENT DATE: 940804 WPI ACCESSION NO.: 94-263767 (9432)
PRIORITY APPLIC. NO.: US 184009 APPLIC. DATE: 940119
NATIONAL APPLIC. NO.: WO 94US888 APPLIC. DATE: 940121
LANGUAGE: English
ABSTRACT: A new attenuated recombinant vaccine (optionally antitumor) has a cytokine and/or tumor -associated antigen (e.g. human tumor necrosis factor, wild-type or mutant nuclear phosphoprotein-p53, human melanoma tumor - associated antigen , interleukin-2, interferon-gamma, interleukin-4, granulocyte -macrophage colony stimulating factor , interleukin-12, B7, erb-B-2 or carcinoembryonic antigen) gene in a non-essential region of vaccinia virus NYVAC or canary-pox virus ALVAC. The C7L-K1L or host range region is deleted, and optionally J2R, B13R + B14R, A26L, A56R, I4L, thymidine-kinase (EC-2.7.1.21), hemorrhagic region, A-type inclusion body, hemagglutinin and/or ribonucleotide-reductase large subunit genes. vP1200, vP1101, vP1098, vP1239, vP1241, vP1237, vP1244, vP1243, vP1248, NYVAC+IFN-gamma+IL-2, vP1250, vP1246, NYVAC+I-12, vP1230, vP1245, NYVAC+IFN-gamma+B7, vP1234, vP1233, vP1100, vP1096, vCP245, vCP235, vCP207, vCP193, vCP275, vCP277, vCP271, vCP278, vCP275+IFN-gamma, vCP277+IFN-gamma, ALVAC+IL-4, vCP290, vCP285, ALVAC+IL-12, vCP268, ALVAC+IFN-gamma+B7, vCP263, vCP267, vCP270, vCP269 and vCP191 are new. (232pp)

3/AB/26 (Item 8 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0165411 DBA Accession No.: 94-07962 PATENT
New immunocomplex of lymphoma tumor-associated antigen and cytokine-recombinant vaccine against B-lymphocyte lymphoma
PATENT ASSIGNEE: Univ.Leland-Stanford-Jr. 1994
PATENT NUMBER: WO 9408601 PATENT DATE: 940428 WPI ACCESSION NO.: 94-150931 (9418)
PRIORITY APPLIC. NO.: US 961788 APPLIC. DATE: 921014
NATIONAL APPLIC. NO.: WO 93US9895 APPLIC. DATE: 931014
LANGUAGE: English
ABSTRACT: A new immunocomplex (A) consists of a B-lymphocyte lymphoma tumor -associated antigen (or epitope-bearing portion) covalently bound to an immune-enhancing cytokine (I). Also new are: DNA encoding (A); a recombinant expression system for producing (A) as a fusion protein; recombinant host cells transformed with this expression system; antibodies (preferably monoclonal antibodies) reactive with the epitope-bearing part of (A) or immunospecific for (A); and any conjugate consisting of (I) covalently bonded to an additional molecular structure. Preferably, the antigen is an immunoglobulin and the epitope-bearing part is the idiotypic region of this Ig. (I) is e.g. granulocyte macrophage colony stimulating factor , interleukin-2 or interleukin-4. (A) is useful in vaccines to protect against proliferation of B-lymphocyte lymphoma. (33pp)

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Set     Items   Description
S1        167   (GM(W)CSF OR GRANULOCYTE(W)MACROPHAGE?(W)COLONY(W)STIMULAT-
            ING(W)(FACTOR? OR ACTIVIT?) OR MACROPHAGE(W)GRANULOCYTE(W)CSF)
             (S)((TUMOR OR TUMOUR OR CANCER?)(W)ASSOCIATED(W)(ANTIGEN OR -
            AG? ?))
S2         56   RD (unique items)
S3         26   S2 AND VACCIN?
S4       6138   (DETECT? OR DIAGN? OR SCEEN? OR DETERMIN? OR DETN)(S)(TUMO-
            R? OR TUMOUR?)(W)ASSOCIATED(W)ANTIGEN?
S5        238   S4 AND ELECTROPHOR?
S6        128   RD (unique items)
S7          0   S1 AND S6
S8          0   S5 AND S1
S9        677   PROTEIN?(W)ARRAY?
S10         0   S4 AND S9
S11     23238   (TUMOR? OR TUMOUR? OR CANCER?)(W)ASSOCIATED(W)(ANTIGEN? OR
            AG)
S12         3   S9 AND S11
S13         3   S12 NOT S3
S14         2   RD (unique items)
?t s4/3 ab/1-2

 4/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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11387379   21314153   PMID: 11421354
 Traveling for the glycosphingolipid path.
  Hakomori S
  Division of Biomembrane Research, Pacific Northwest Research Institute,
Seattle, WA 98122, USA. hakomori@u.washington.edu
  Glycoconjugate journal (United States) Jul-Sep 2000, 17 (7-9)
 p627-47, ISSN 0282-0080 Journal Code: BJJ
  Languages: ENGLISH
  Document type: Journal Article
  Record type: In Process
  Our studies on glycosphingolipids (GSLs) were initiated through isolation
and structural characterization of lacto-series type 1 and 2 GSLs, and
globo-series GSLs. Lacto-series structures included histo-blood group ABH
and I/i antigens. Our subsequent studies were focused on GSL changes
associated with: (i) ontogenic development and differentiation; (ii)
oncogenic transformation and tumor progression. Various novel types of GSLs
such as extended globo-series, sialyl-Le(x) (SLe(x)), sialyl-dimeric-Le(x)
(SLe(x)-Le(x)), dimeric-Le(x) (Le(x)-Le(x)), Le(y)-on-Le(x), dimeric-Le(a)
(Le(a)-Le(a)), Le(b)-on-Le(a), etc. were identified as tumor -associated
  antigens . These studies provide an essential basis for up- or
down-regulation of key glycosyltransferase genes controlling development,
differentiation, and oncogenesis. GSL structures established in our
laboratory are summarized in Table 1, and structural changes of GSLs
associated with ontogenesis and oncogenesis are summarized in Sections 2
and 3. Based on these results, we endeavored to find out the cell
biological significance of GSL changes, focused on (i) cell adhesion, e.g.,
the compaction process of preimplantation embryo in which Le(x)-to-Le(x),
Gb4-to-GalGb4 or -nLc4 play major roles; and (ii) modulation of signal
transduction through interaction of growth factor receptor tyrosine kinase
with ganglioside, e.g., EGF receptor tyrosine kinase with GM3. Recent
trends of studies on i and ii lead to the concept that GSL clusters
(microdomains) are organized with various signal transducer molecules to
form 'glycosignaling domains' (GSD). GSL-dependent adhesion occurs through
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clustered GSLs, and is coupled with activation of signal transducers (cSrc, Src family kinase, Rho A, etc.). Clustered GSLs involved in cell adhesion are recognized by GSLs on counterpart cells (carbohydrate-to-carbohydrate interaction), or by lectins (e.g., siglecs, selectins). Our major effort in utilization of GSLs in medical science has been for: (i) cancer diagnosis and treatment (vaccine development) based on tumor-associated GSLs and glycoepitopes; (ii) genetically defined phenotype for susceptibility to E. coli infection; (iii) clear identification of physiological E-selectin epitope (myeloglycan) expressed on neutrophils and myelocytes; (iv) characterization of sialyl poly-LacNAc epitopes recognized as male-specific antigens. Utilization of these GSLs or glycoepitopes in development of anti-adhesion approach to prevent tumor metastasis, infection, inflammation, or fertilization (i.e., contraceptive) is discussed. For each approach, development of mimetics of key GSLs or glycoepitopes is an important subject of future study.

4/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11383442 21311485 PMID: 11418297
Immunocytochemical detection of leukocyte-associated and apoptosis-related antigen expression in childhood brain tumors.
Bodey B; Bodey B; Siegel SE; Kaiser HE
Department of Pathology, University of Southern California, 8000-1 Canby Avenue, Reseda, Los Angeles, CA, USA
Critical reviews in oncology/hematology (Ireland) Aug 2001, 39 (1-2) p3-16, ISSN 1040-8428 Journal Code: AGO
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
During systematic cell-surface antigen expression profile analyses of 76 primary childhood brain tumors [34 medulloblastomas (MED)/primitive neuroectodermal tumors (PNETs) and 42 astrocytomas (ASTR)], a library of monoclonal antibodies (MoABs) directed against various leukocyte-associated, lymphocyte cell-line differentiation antigens in childhood brain tumors was utilized. The antigens were detected employing an indirect, biotin-streptavidin conjugated alkaline phosphatase (AP) immunocytochemical technique. Major histocompatibility complex (MHC) class I restricted, tumor - associated antigen (TAA) specific, CD8(+) cytotoxic T lymphocytes (CTL) were identified in 58/76 (76.32%) brain tumors, and usually represented 1-10% of all cells, but in some cases 30-44% of the cells were CD8(+). CD4(+), MHC class II restricted helper lymphocytes were present in 65/76 (85.53%) brain tumors, and accounted for 1-10% of the observed cells. Macrophages were present in 74/76 (97.37%) brain tumors, and their number also represented 1-10% of all observed cells in the brain tumor frozen sections. Leukocyte common antigen (LCA) expression was detected in all 76 (100%) brain tumors studied. MoAB UJ 308 detected the presence of premyelocytes and mature granulocytes in 60/76 (78.95%) brain tumors. Natural killer (NK) cells were not defined in the observed brain tumors. The great majority of childhood glial tumors, particularly ASTRs express Fas (APO-1/CD95) receptor whereas normal cells in the central nervous system (CNS) do not. FasR is a transmembrane glycoprotein which belongs to the nerve growth factor/tumor necrosis factor (NGF/TNF) receptor superfamily. As part of our screening, the 42 childhood ASTRs were also investigated for expression of CD95. We detected strong expression (strong intensity of staining, number of stained cells 50-100%) of FasR, employing formalin fixed, paraffin-wax embedded tissue slides. Brain tumors and melanomas have been shown to produce their autocrine FasL, and are even capable of switching CD95-related signal transduction from the

PCD pathway to a proliferative pathway. In view of our results, we conclude that: (1) the tumor infiltrating leukocytes in MEDs/PNETs and ASTRs represent a very diverse population and are present in a great majority of the cases studied; (2) the strong expression of FasR in ASTRs provides a manner in which T lymphocytes may exert their anti-tumor effects, but may also represent yet another way that tumors may evade the immune response; and (3) further observations of the expression of various antigens involved in juxtacrine, in situ growth control are necessary for the refinement of cellular immunotherapeutical approaches in the treatment of human malignancies.
?t s14/3 ab/1-2

14/AB/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04585980 Genuine Article#: TU634 Number of References: 68
Title: TOWARD SELECTIVE ELICITATION OF T(H)1-CONTROLLED VACCINATION RESPONSES - VACCINE APPLICATIONS OF BACTERIAL SURFACE-LAYER PROTEINS (Abstract Available)
Author(s): JAHNSCHMID B; MESSNER P; UNGER FM; SLEYTR UB; SCHEINER O; KRAFT D
Corporate Source: AGR UNIV VIENNA,ZENTRUM ULTRASTRUKTURFORSCH,GREGOR MENDEL STR 33/A-1180 VIENNA//AUSTRIA/; AGR UNIV VIENNA,ZENTRUM ULTRASTRUKTURFORSCH/A-1180 VIENNA//AUSTRIA/; AGR UNIV VIENNA,LUDWIG BOLTZMANN INST MOLEK NANOTECHNOL/A-1180 VIENNA//AUSTRIA/; UNIV VIENNA,INST ALLGEMEINE & EXPTL PATHOL/A-1090 VIENNA//AUSTRIA/
Journal: JOURNAL OF BIOTECHNOLOGY, 1996, V44, N1-3 (JAN 26), P225-231
ISSN: 0168-1656
Language: ENGLISH Document Type: ARTICLE
Abstract: Bacterial surface layer proteins have been utilized as combined vaccine carrier/adjuvants and offer a number of advantages in these applications. The crystalline protein arrays contain functional groups in precisely defined orientations for coupling of haptens. Conventional applications of S-layer vaccines do not cause observable trauma or side effects. Depending on the nature of the S-layer preparations, antigenic conjugates will induce immune responses of a predominantly cellular or predominantly humoral nature. Immune responses to S-layer-hapten conjugates are also observed following oral/nasal application. In the present contribution, the status of investigations with S-layer conjugates in three main immunological projects is reviewed. In a project aimed at immunotherapy of cancer, conjugates of S-layer with small, tumor-associated oligosaccharides have been found to elicit hapten-specific DTH responses. An enlarged program of chemical synthesis has now been initiated to prepare a complete set of mucin-derived, tumor-associated oligosaccharides and their chemically modified analogues for elicitation of cell-mediated immune responses to certain tumors in humans. In another application, oligosaccharides derived from capsules of Streptococcus pneumoniae type 8 have been linked to S-layer proteins and have been found to elicit protective antibody responses in animals. Most recently, allergen-S-layer conjugates have been prepared with the intention to suppress the T(H)2-directed, IgE-mediated allergic responses to Bet nu 1, the major allergen of birch pollen. In the former two applications, the S-layer vaccine technology appears to offer the versatility needed to direct vaccination responses toward predominant control by T(H)1 or T(H)2 lymphocytes to meet the different therapeutic or prophylactic requirements in each case. In the third application, work has progressed to a preliminary stage only.

14/AB/2 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

013193879
WPI Acc No: 2000-365752/200031
XRAM Acc No: C00-110573
XRPX Acc No: N00-273655
Treating and diagnosing cancer comprises contacting serum samples obtained before and after vaccine treatment with an array of proteins from a biological sample
Patent Assignee: CELL GENESYS INC (CELL-N)
Inventor: ANDO D; CHANG J; MCARTHUR J; ROBERTS M; SIMONS J
Number of Countries: 080 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200026676	A1	20000511	WO 99US25936	A	19991103	200031	B
AU 200013409	A	20000522	AU 200013409	A	19991103	200040	

Priority Applications (No Type Date): US 98106795 A 19981103
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200026676	A1	E	92	G01N-033/68	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200013409	A		G01N-033/68	Based on patent WO 200026676

Abstract (Basic): WO 200026676 A1
Abstract (Basic):
NOVELTY - A method for obtaining a tumor -associated antigen (TAA) is new.
DETAILED DESCRIPTION - The method comprises;
(a) preparing an array of proteins from a biological sample;
(b) obtaining a first and second serum sample from a subject before and after, respectively, treatment with a vaccine comprising proliferation incompetent tumor cells expressing GM-CSF and the TAA;
(c) contacting a first sample of the proteins in (a) with the first serum sample;
(d) contacting a second sample of the proteins in (a) with the second serum sample; and
(e) identifying a protein in the array that reacts with the second serum sample but not the first.
INDEPENDENT CLAIMS are also included for the following;
(1) screening for the presence of a TAA comprising;
(a) isolating the TAA identified in the method above;
(b) preparing an antibody against TAA;
(c) contacting the biological specimen with the antibody in (b); and
(d) detecting the presence of an antigen-antibody complex.
(2) a kit for screening the presence of a TAA in a biological sample comprising;
(a) unlabelled first antibodies against a TAA reactive with serum from an individual treated with a vaccine comprising proliferation incompetent tumor cells expressing the TAA and GM-CSF, but not reactive with a pre-treatment serum sample;
(b) a solid support for adhering the biological sample; and
(c) labelled second antibodies against the first antibodies.

ACTIVITY - Cytostatic; antiproliferative.

MECHANISM OF ACTION - The vaccine increases the expression of the tumor associated antigens and enables the identification of tumor cells by the immune system of the affected individual. No data given.

USE - The method is useful for the identification of tumor - associated antigens .

DESCRIPTION OF DRAWING(S) - The drawing is a schematic representation of the MFG vector containing a cytokine-encoding sequence.

pp; 92 DwgNo 1/18

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